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=> d his

     (FILE 'HOME' ENTERED AT 14:36:01 ON 09 NOV 2009)

     FILE 'REGISTRY' ENTERED AT 14:36:26 ON 09 NOV 2009
L1             1 S 132539-06-1/RN
L2             1 S OLANZAPINE/CN

     FILE 'REGISTRY' ENTERED AT 14:38:01 ON 09 NOV 2009
L3               STR 132539-06-1
L4           110 S L3 FAM FUL

     FILE 'CAPLUS' ENTERED AT 14:38:21 ON 09 NOV 2009
L5             1 S US20080161557/PN
                 SELECT RN L5 1-

     FILE 'REGISTRY' ENTERED AT 14:38:37 ON 09 NOV 2009
L6            27 S E1-27
L7             4 S L4 AND L6
L8            23 S L6 NOT L7
L9             2 S L8 AND 5-6-7/SZ
L10            1 S L9 AND NRS=2
L11            1 S L9 NOT L10
L12           21 S L8 NOT L9
L13            2 S L12 AND SULF?
L14            6 S L12 AND ACID
L15           13 S L12 NOT (L13 OR L14)

     FILE 'CAPLUS' ENTERED AT 14:55:14 ON 09 NOV 2009
L16         2989 S L7
L17           65 S L11
L18           56 S L10
L19        43364 S L13
L20       138814 S L14
L21       344068 S L15
L22           60 S L16 AND L17
L23           55 S L16 AND L18
L24           41 S L16 AND L19
L25           48 S L16 AND L20
L26           94 S L16 AND L21
L27          123 S L24 OR L25 OR L26
L28          105 S L22 OR L23
L29           27 S L27 AND L28

=> d ibib abs hitstr total
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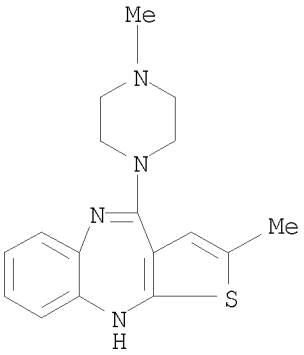
L29 ANSWER 1 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:537811 CAPLUS
DOCUMENT NUMBER: 148:561947
TITLE: Preparation of olanzapine
INVENTOR(S): Wu, Jianjun; Li, Aopan; Ma, Shining; Li, Mingchuan
PATENT ASSIGNEE(S): Southwest Synthetic Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 6pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 101168544	A	20080430	CN 2007-10092995	20071116

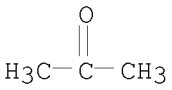
PRIORITY APPLN. INFO.: CN 2007-10092995 20071116
OTHER SOURCE(S): CASREACT 148:561947

AB In this invention, olanzapine is prepared by dissolving 2-methyl-4-amino-10H-thieno[2,3-b][1,5]benzodiazepine salt in solvent, adding N,N-bis(2-haloethyl)methylamine and basic catalyst, reacting at 50-120°C for 2-10 h, cooling the reaction mixture, adding water or mixture of water and methanol till precipitate is formed, filtering, washing with solvent, and vacuum-drying. The product has high yield.

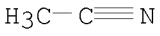
IT 132539-06-1P, Olanzapine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of olanzapine by cyclization of aminothienobenzodiazepine salt with bis(haloethyl)methylamine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 67-64-1, Acetone, uses 75-05-8, Acetonitrile, uses 109-99-9, Thf, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of olanzapine by cyclization of aminothienobenzodiazepine salt with bis(haloethyl)methylamine)
RN 67-64-1 CAPLUS
CN 2-Propanone (CA INDEX NAME)

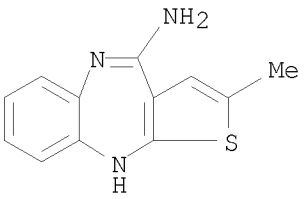


RN 75-05-8 CAPLUS
CN Acetonitrile (CA INDEX NAME)



RN 109-99-9 CAPLUS
CN Furan, tetrahydro- (CA INDEX NAME)

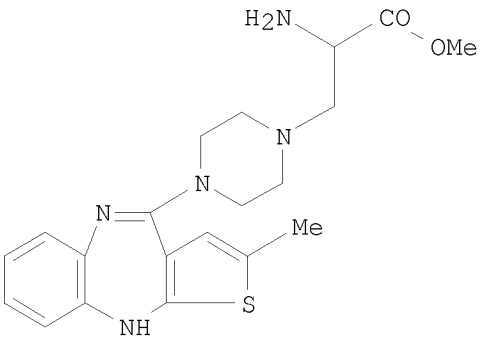
IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of olanzapine by cyclization of aminothienobenzodiazepine salt with bis(haloethyl)methylamine)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



L29 ANSWER 2 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:529197 CAPLUS
DOCUMENT NUMBER: 148:495988
TITLE: Preparation of novel psychotropic agents comprising CNS active and NMDA receptor modulator moieties
INVENTOR(S): Portnoy, Moshe; Gil-Ad, Irit; Weizman, Avraham
PATENT ASSIGNEE(S): Ramot at Tel-Aviv University Ltd, Israel
SOURCE: PCT Int. Appl., 89pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008050341	A2	20080502	WO 2007-IL1296	20071025
WO 2008050341	A3	20080619		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
EP 2077860	A2	20090715	EP 2007-827270	20071025
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR				
IN 2009MN01015	A	20090612	IN 2009-MN1015	20090525
PRIORITY APPLN. INFO.:			US 2006-854091P P	20061025
			WO 2007-IL1296 W	20071025

OTHER SOURCE(S): MARPAT 148:495988
GI



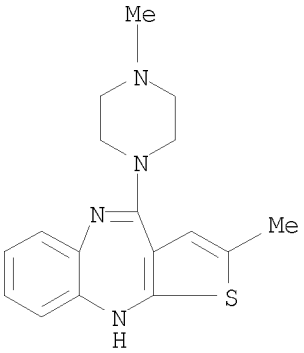
I

AB The invention provides novel compds. and pharmaceutical compns. for the treatment of psychol. and/or psychiatric diseases or disorders. The compds. of the invention, or salts, prodrugs, or stereoisomers thereof, are of general formula L-M-V, wherein L is a CNS active moiety; M is a linker; and V is a modulator of the glutamate NMDA receptor. The CNS active moiety is derived from CNS active compds. selected from an anticonvulsant drug, an anti-Parkinsonian drug, an opioid and non-opioid analgesic, an appetite suppressant, an antiemetic, an analgesic-antipyretic, a stimulant, an antidepressant, an antimanic agent, an antianxiety agent, an antipsychotic agent, a sedative, and a hypnotic. Such agents are useful in the treatment of schizophrenia and bipolar depression, and in particular have the ability to alter the neg. symptoms of schizophrenia. Such novel agents are also useful in altering states of other mood disorders such as depression and anxiety, cognitive deficits, movement disorders, and drug addiction. Synthesis of the compds. is exemplified. Example compound I was prepared in a multistep synthesis involving ring closure of 2-(2-nitroanilido)-5-methyl-3-thiophenecarbonitrile (preparation given), subsequent reaction with piperazine and Boc-iodo-Ala-OMe. In various animal model screening tests, I exhibited anxiolytic activity, efficacy against psychotic symptoms, and antidepressant activity.

IT 132539-06-1, Olanzapine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CNS moiety; preparation of novel psychotropic agents comprising CNS active and NMDA receptor modulator moieties)

RN 132539-06-1 CAPLUS

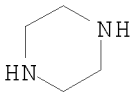
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 110-85-0, Piperazine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of novel psychotropic agents comprising CNS active and NMDA receptor modulator moieties)

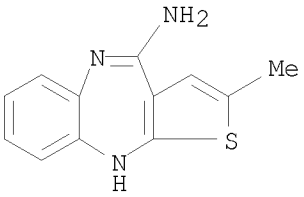
RN 110-85-0 CAPLUS

CN Piperazine (CA INDEX NAME)



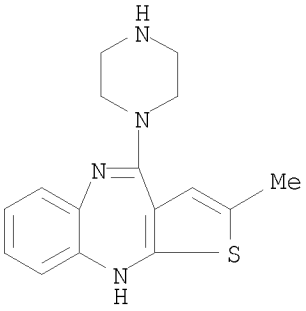
IT 138564-60-0P, 4-Amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride 161696-76-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of novel psychotropic agents comprising CNS active and NMDA receptor modulator moieties)

RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



L29 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:10517 CAPLUS
DOCUMENT NUMBER: 148:93259
TITLE: Use of n-desmethylclozapine to treat psychosis
INVENTOR(S): Weiner, David; Van Kammen, Daniel P.; Corritori, Suzana
PATENT ASSIGNEE(S): Acadia Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 88pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008002602	A1	20080103	WO 2007-US14897	20070626

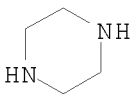
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-817010P P 20060627

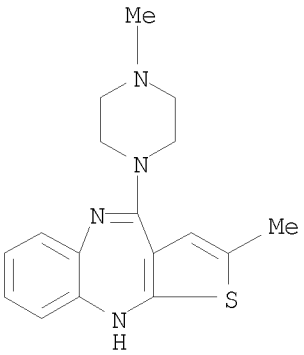
AB Disclosed herein is are methods to treat neuropsychiatric diseases including psychosis. Treatment is carried out by administering a therapeutically effective amount of N-desmethylclozapine to a patient suffering from a neuropsychiatric disease.

IT 110-85-0, Piperazine, biological studies 132539-06-1, Olanzapine 161696-76-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(desmethylclozapine to treat psychosis)

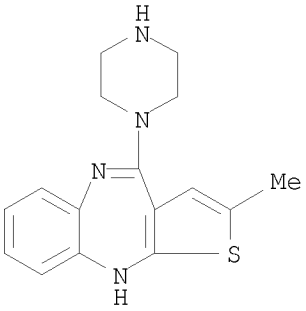
RN 110-85-0 CAPLUS
CN Piperazine (CA INDEX NAME)



RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:819070 CAPLUS
DOCUMENT NUMBER: 147:197377
TITLE: Novel polymorph E of olanzapine and preparation of anhydrous non-solvated crystalline polymorphic form I of 2-methyl-4(4-methyl-1-piperazinyl)-10h-thieno[2,3-b][1,5] benzodiazepine (olanzapine form i) from the polymorphic olanzapine form e
INVENTOR(S): Ray, Anup Kumar; V. Patel, Hiren Kumar; Ludescher, Johannes; Patel, Mahendra R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 13pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070173496	A1	20070726	US 2006-340284	20060126
WO 2007087555	A2	20070802	WO 2007-US60958	20070124
WO 2007087555	A3	20071025		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2006-340284 A 20060126

AB The invention provides an Olanzapine pseudopolymoph Form E. The invention provides methods of preparing polymorphic Olanzapine Form E employing rapid crystallization and seeding. The invention provides methods of preparing anhydrous Olanzapine Form I from the Olanzapine Form E by step-wise drying.

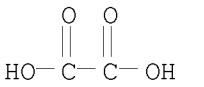
IT 67-68-5, Dimethyl sulfoxide, analysis 141-78-6, Ethyl acetate, analysis 144-62-7, Oxalic acid, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(polymorph E of olanzapine and preparation of anhydrous non-solvated crystalline polymorphic form I of 2-methyl-4(4-methyl-1-piperazinyl)-10h-thieno[2,3-b][1,5] benzodiazepine (olanzapine form I) from polymorphic olanzapine form E)

RN 67-68-5 CAPLUS
CN Methane, 1,1'-sulfinylbis- (CA INDEX NAME)

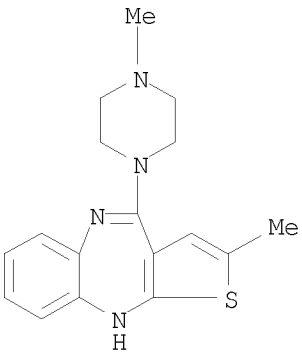
RN 141-78-6 CAPLUS
CN Acetic acid ethyl ester (CA INDEX NAME)

Et—O—Ac

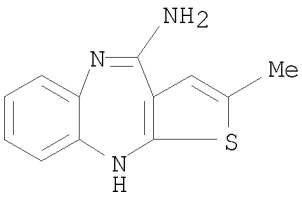
RN 144-62-7 CAPLUS
CN Ethanedioic acid (CA INDEX NAME)



IT 132539-06-1P, Olanzapine
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polymorph E of olanzapine and preparation of anhydrous non-solvated crystalline
polymorphic form I of 2-methyl-4(4-methyl-1-piperazinyl)-10h-thieno[2,3-b][1,5] benzodiazepine (olanzapine form I) from polymorphic olanzapine form E)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(polymorph E of olanzapine and preparation of anhydrous non-solvated crystalline
polymorphic form I of 2-methyl-4(4-methyl-1-piperazinyl)-10h-thieno[2,3-b][1,5] benzodiazepine (olanzapine form I) from polymorphic olanzapine form E)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

L29 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:761505 CAPLUS
DOCUMENT NUMBER: 147:150819
TITLE: Method for preparing a mixed solvate of olanzapine
INVENTOR(S): Dalmases Barjoan, Pere; Herbera Espinal, Reyes
PATENT ASSIGNEE(S): Inke, S.A., Spain
SOURCE: PCT Int. Appl., 17pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

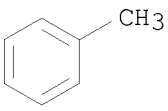
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007077134	A1	20070712	WO 2006-EP70028	20061220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
ES 2292333	A1	20080301	ES 2006-59	20060105
ES 2292333	B1	20081216		
EP 1968983	A1	20080917	EP 2006-841525	20061220
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS				
JP 2009522319	T	20090611	JP 2008-548969	20061220
KR 2008107359	A	20081210	KR 2008-719172	20080805

PRIORITY APPLN. INFO.:			
	ES 2006-59	A	20060105
	ES 2004-1850	A0	20040727
	WO 2006-EP70028	W	20061220

AB An improved method is provided for preparing a mixed solvate of olanzapine/water/tetrahydrofuran in a proportion of 1:1:1/2. The improvement is characterized in that the mixed solvate is basically prepared by means of methylation of the N-desmethylolanzapine with di-Me sulfate, using THF and water as solvents.

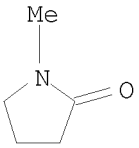
IT 108-88-3, Toluene, uses 109-99-9, Tetrahydrofuran, uses 872-50-4, N-Methylpyrrolidone, uses
RL: NUU (Other use, unclassified); USES (Uses)
(method for preparing mixed solvate of olanzapine)

RN 108-88-3 CAPLUS
CN Benzene, methyl- (CA INDEX NAME)

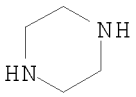


RN 109-99-9 CAPLUS
CN Furan, tetrahydro- (CA INDEX NAME)

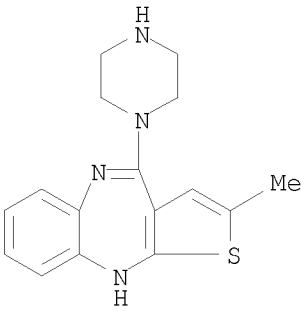
RN 872-50-4 CAPLUS
CN 2-Pyrrolidinone, 1-methyl- (CA INDEX NAME)



IT 110-85-0, Piperazine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for preparing mixed solvate of olanzapine)
RN 110-85-0 CAPLUS
CN Piperazine (CA INDEX NAME)



IT 161696-76-0P, N-Demethylolanzapine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for preparing mixed solvate of olanzapine)
RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)

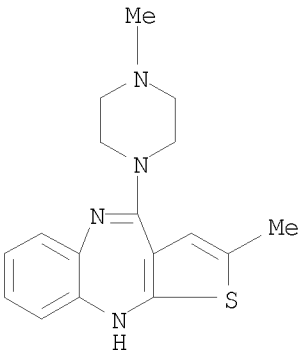


IT 132539-06-1P, Olanzapine
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
USES (Uses)
(method for preparing mixed solvate of olanzapine)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-
(CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:538023 CAPLUS
DOCUMENT NUMBER: 146:507833
TITLE: Process for the preparation of olanzapine for dosage forms
INVENTOR(S): Kovanyine Lax, Gyoergyi; Nemeth, Gabor; Krasznai, Gyoergy; Mesterhazy, Norbert; Nagy, Kalman; Vereczkeyne Donath, Gyoergyi; Szent-Kirallyi, Zsuzsanna
PATENT ASSIGNEE(S): Egis Gyogyszergyar Nyrt., Hung.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007054750	A2	20070518	WO 2006-HU96	20061110
WO 2007054750	A3	20071011		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
HU 2005001046	A2	20070828	HU 2005-1046	20051111
EP 1963335	A2	20080903	EP 2006-808805	20061110
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
EP 1997822	A1	20081203	EP 2008-13602	20061110
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
JP 2009515867	T	20090416	JP 2008-539513	20061110
IN 2008DN03939	A	20080711	IN 2008-DN3939	20080507
CN 101400683	A	20090401	CN 2006-80041817	20080509
NO 2008002503	A	20080811	NO 2008-2503	20080603
US 20090137563	A1	20090528	US 2008-93344	20081002

PRIORITY APPLN. INFO.:

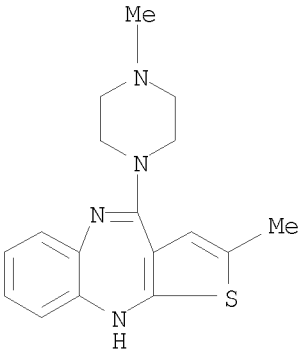
HU 2005-1046	A	20051111
EP 2006-808805	A3	20061110
WO 2006-HU96	W	20061110

AB The invention relates to a process for the preparation of olanzapine by reacting 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride with N-methylpiperazine in an organic solvent having good phys. properties and suitable in respect of environmental and labour safety consideration, i.e., a mixture of toluene and 1,3-dimethyl-2-imidazolidinone. The invention also encompasses novel olanzapine dihydrochloride trihydrate, the preparation thereof and

pharmaceutical compns. comprising the novel compound

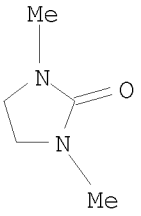
IT 132539-06-1P, Olanzapine
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of olanzapine using aminomethylthienobenzodiazepine for dosage forms)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

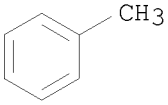


IT 80-73-9, 1,3-Dimethyl-2-imidazolidinone 108-88-3, Toluene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of olanzapine using aminomethylthienobenzodiazepine for dosage forms)

RN 80-73-9 CAPLUS
CN 2-Imidazolidinone, 1,3-dimethyl- (CA INDEX NAME)



RN 108-88-3 CAPLUS
CN Benzene, methyl- (CA INDEX NAME)

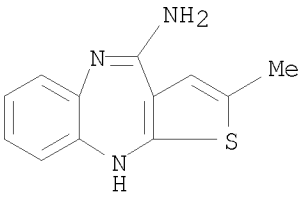


IT 138564-60-0, 4-Amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of olanzapine using aminomethylthienobenzodiazepine for dosage forms)

RN 138564-60-0 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)

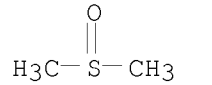


● HCl

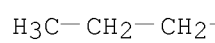
L29 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:412748 CAPLUS
DOCUMENT NUMBER: 148:175622
TITLE: An improved process for the preparation of olanzapine form I
INVENTOR(S): Ray, Uttam Kumar; Rao, Pathuri Sreenivasa; Sivakumaran, Meenakshisunderam
PATENT ASSIGNEE(S): Aurobindo Pharma Limited, India
SOURCE: Indian Pat. Appl., 11pp.
CODEN: INXXBQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 2005CH00188	A	20070316	IN 2005-CH188	20050301
WO 2007138376	A1	20071206	WO 2006-IB1769	20060601
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20090131658	A1	20090521	US 2008-227819	20081129
PRIORITY APPLN. INFO.:			IN 2005-CH188	T0 20050301
			WO 2006-IB1769	W 20060601

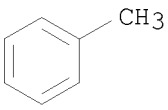
OTHER SOURCE(S): CASREACT 148:175622
AB An improved for preparing olanzapine form I of formula I in the presence of one solvent or a mixture of solvents.
IT 67-68-5, Dimethyl sulfoxide, uses 71-36-3, Butanol, uses 108-88-3, Toluene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(improved process for preparation of olanzapine form I)
RN 67-68-5 CAPLUS
CN Methane, 1,1'-sulfinylbis- (CA INDEX NAME)



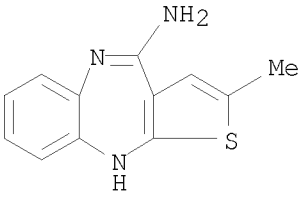
RN 71-36-3 CAPLUS
CN 1-Butanol (CA INDEX NAME)



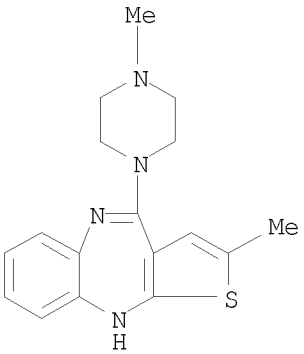
RN 108-88-3 CAPLUS
CN Benzene, methyl- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(improved process for preparation of olanzapine form I)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



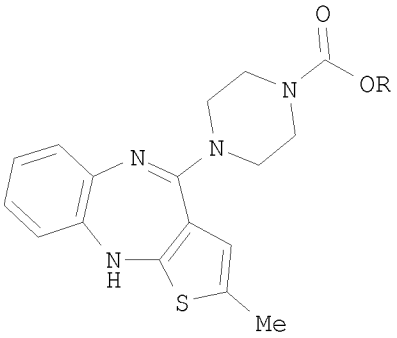
IT 132539-06-1P, Olanzapine
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(improved process for preparation of olanzapine form I)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



L29 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:265943 CAPLUS
DOCUMENT NUMBER: 146:380021
TITLE: Preparation and application of Olanzapine intermediate
INVENTOR(S): Tang, Chaojun; Yao, Chengzhi; Jia, Cunchao
PATENT ASSIGNEE(S): Hangzhou Shengmei Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 13pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

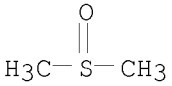
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1923834	A	20070307	CN 2006-10053509	20060911
CN 100383144	C	20080423		

PRIORITY APPLN. INFO.: CN 2006-10053509 20060911
OTHER SOURCE(S): CASREACT 146:380021; MARPAT 146:380021
GI



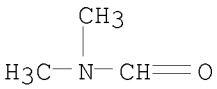
I

AB The title Olanzapine intermediate has a general formula I (R = C1-C6 alkyl, C6-C18 aryl, heteroaryl, or benzyl). This Olanzapine intermediate can be used to prepare Olanzapine with the advantages of high Olanzapine yield, safe operation, low pollution on environment, etc.
IT 67-68-5, DMSO, uses 68-12-2, DMF, uses
108-88-3, Toluene, uses 109-99-9, THF, uses
127-19-5, N,N-Dimethylacetamide
RL: NUU (Other use, unclassified); USES (Uses)
(preparation and application of Olanzapine intermediate)
RN 67-68-5 CAPLUS
CN Methane, 1,1'-sulfinylbis- (CA INDEX NAME)

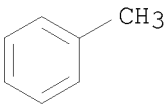


RN 68-12-2 CAPLUS

CN Formamide, N,N-dimethyl- (CA INDEX NAME)

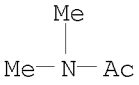


RN 108-88-3 CAPLUS
CN Benzene, methyl- (CA INDEX NAME)

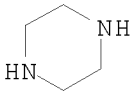


RN 109-99-9 CAPLUS
CN Furan, tetrahydro- (CA INDEX NAME)

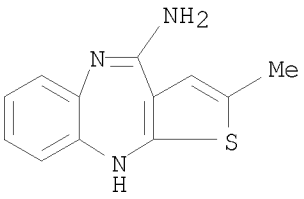
RN 127-19-5 CAPLUS
CN Acetamide, N,N-dimethyl- (CA INDEX NAME)



IT 110-85-0, Piperazine, reactions 138564-60-0
161696-76-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and application of Olanzapine intermediate)
RN 110-85-0 CAPLUS
CN Piperazine (CA INDEX NAME)

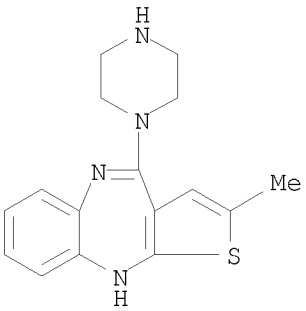


RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)

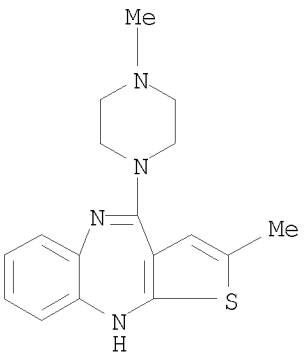


● HCl

RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



IT 132539-06-1P, Olanzapine
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and application of Olanzapine intermediate)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

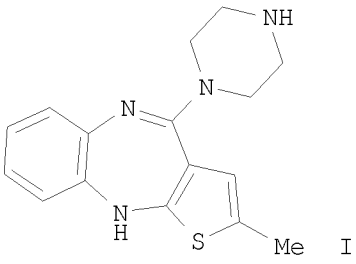


L29 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:494300 CAPLUS
DOCUMENT NUMBER: 145:8200
TITLE: A process for the preparation of N-demethylolanzapine
INVENTOR(S): Stawinski, Tomasz; Rechnio, Justyna; Majka, Zbigniew
PATENT ASSIGNEE(S): Adamed Sp. z o.o., Pol.
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

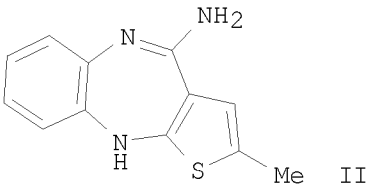
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006053870	A1	20060526	WO 2005-EP55981	20051115
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PL 198589	B1	20080630	PL 2004-371307	20041122
EP 1814886	A1	20070808	EP 2005-810971	20051115
EP 1814886	B1	20081022		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
CN 101061124	A	20071024	CN 2005-80039962	20051115
EP 1988092	A1	20081105	EP 2008-161324	20051115
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
AT 412000	T	20081115	AT 2005-810971	20051115
ES 2315928	T3	20090401	ES 2005-810971	20051115
NO 2007003165	A	20070622	NO 2007-3165	20070622

PRIORITY APPLN. INFO.:			
	PL 2004-371307	A	20041122
	EP 2005-810971	A3	20051115
	WO 2005-EP55981	W	20051115

OTHER SOURCE(S): CASREACT 145:8200
GI



I



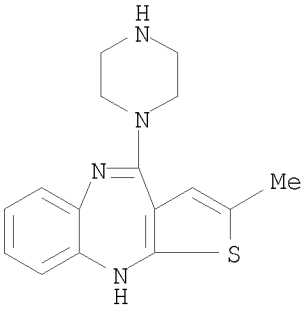
II

AB The invention relates to the process for the preparation of N-demethylolanzapine I and the use of N-demethylolanzapine obtained by the process for the preparation of antipsychotic medicament olanzapine. According to the process of the invention the reaction of anhydrous piperazine with 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine II or its inorg. acid addition salt is carried out in molten piperazine, in the absence of a solvent.

IT 161696-76-0P, N-Demethylolanzapine
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for the preparation of N-demethylolanzapine)

RN 161696-76-0 CAPLUS

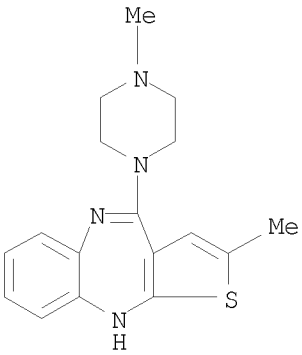
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



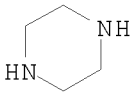
IT 132539-06-1P, Olanzapine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of N-demethylolanzapine)

RN 132539-06-1 CAPLUS

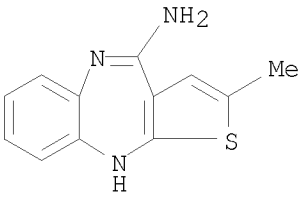
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 110-85-0, Piperazine, reactions 138564-60-0,
4-Amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the preparation of N-demethylolanzapine)
RN 110-85-0 CAPLUS
CN Piperazine (CA INDEX NAME)



RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride
(1:1) (CA INDEX NAME)



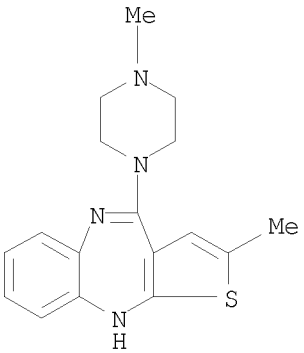
● HCl

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:149063 CAPLUS
DOCUMENT NUMBER: 144:212809
TITLE: Process for preparing olanzapine via methylation of N-demethylolanzapine in dichloromethane and/or methanol.
INVENTOR(S): Venkataraman, Sundaram; Rajan, Srinivasan Thirumalai; Bulusu, Veera Venkata Naga Chandra Sekhar; Kasturi, Ravi Kumar; Kapabalu, Suneel Kumar; Gokavalasa, Kavitha
PATENT ASSIGNEE(S): Dr. Reddy's Laboratories Limited, India
SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

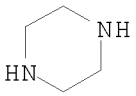
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20060035887	A1	20060216	US 2005-171093		20050630
PRIORITY APPLN. INFO.:			US 2004-585198P	P	20040702

OTHER SOURCE(S): CASREACT 144:212809
AB A process for preparing olanzapine comprises methylation of N-demethylolanzapine with a methylating agent in a solvent comprising CH2Cl2, MeOH, or a mixture thereof. Thus, N-demethylolanzapine (preparation given) in CH2Cl2 at <0° was treated with Me2SO4 and then with NaOH in MeOH at 0-5° to give olanzapine of 99.8% purity.
IT 132539-06-1P, Olanzapine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparing olanzapine via methylation of N-demethylolanzapine in dichloromethane and/or methanol)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

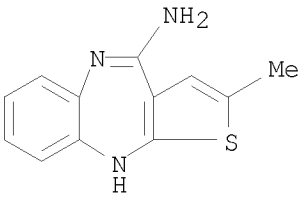


IT 110-85-0, Piperazine, reactions 138564-60-0, 4-Amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparing olanzapine via methylation of N-demethylolanzapine in dichloromethane and/or methanol)

RN 110-85-0 CAPLUS
CN Piperazine (CA INDEX NAME)

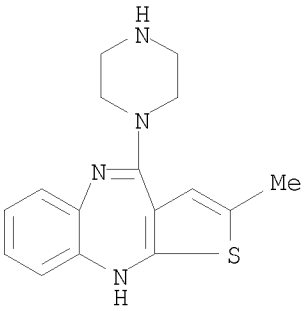


RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

IT 161696-76-0P, N-Demethylolanzapine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparing olanzapine via methylation of N-demethylolanzapine in dichloromethane and/or methanol)
RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



L29 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:117133 CAPLUS
DOCUMENT NUMBER: 144:198861
TITLE: Mixed solvate of olanzapine, method for preparing it and method for preparing form I of olanzapine therefrom
INVENTOR(S): Dalmases Barjoan, Pere; Bessa Bellmunt, Jordi
PATENT ASSIGNEE(S): Laboratorios Lesvi, S.L., Spain
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006013435	A1	20060209	WO 2005-IB2209	20050707
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
ES 2253091	A1	20060516	ES 2004-1850	20040727
ES 2253091	B1	20070201		
EP 1773841	A1	20070418	EP 2005-759149	20050707
EP 1773841	B1	20071205		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
AT 380191	T	20071215	AT 2005-759149	20050707
JP 2008508254	T	20080321	JP 2007-523170	20050707
ES 2299049	T3	20080516	ES 2005-759149	20050707
ZA 2007000670	A	20080827	ZA 2007-670	20050707
US 20080280884	A1	20081113	US 2006-568021	20061017
IN 2006DN06347	A	20070831	IN 2006-DN6347	20061030
KR 2007063496	A	20070619	KR 2007-702091	20070126

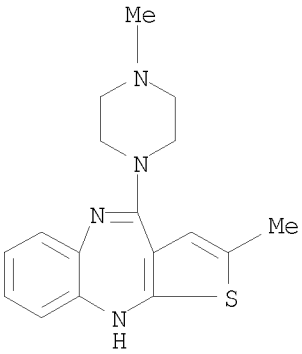
PRIORITY APPLN. INFO.: ES 2004-1850 A 20040727
WO 2005-IB2209 W 20050707

AB Said mixed solvate is a solvate of olanzapine/water/tetrahydrofuran in the proportion 1:1:1/2 (I). The method for preparing said solvate comprises treating a crude anhydrous olanzapine with a mixture of tetrahydrofuran/water. The method for preparing Form I of olanzapine includes desolvating the mixed solvate of formula I, by means of drying, in vacuo and under temperature-controlled conditions.

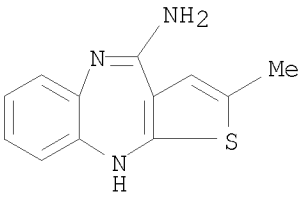
IT 109-99-9, Tetrahydrofuran, reactions 132539-06-1, Olanzapine 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(mixed solvate of olanzapine and method for preparing form I of olanzapine therefrom)

RN 109-99-9 CAPLUS
CN Furan, tetrahydro- (CA INDEX NAME)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-
(CA INDEX NAME)



RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride
(1:1) (CA INDEX NAME)

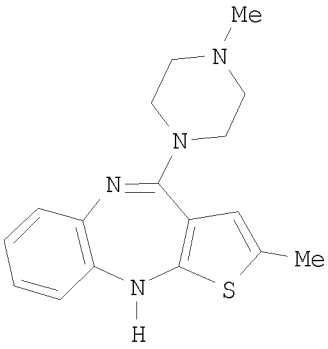


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:54122 CAPLUS
DOCUMENT NUMBER: 144:150401
TITLE: A process for the preparation of olanzapine
INVENTOR(S): Shastri, Jwalant Ashesh; Bhatnagar, Akshat; Thaper, Rajesh Kumar; Dubey, Sushil Kumar
PATENT ASSIGNEE(S): Jubilant Organosys Ltd., India
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006006180	A1	20060119	WO 2004-IN207	20040714
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2576862	A1	20060119	CA 2004-2576862	20040714
EP 1778649	A1	20070502	EP 2004-745138	20040714
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
WO 2007105225	A1	20070920	WO 2006-IN91	20060314
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20090005556	A1	20090101	US 2008-632362	20080818
PRIORITY APPLN. INFO.:			WO 2004-IN207 W	20040714

OTHER SOURCE(S): CASREACT 144:150401
GI



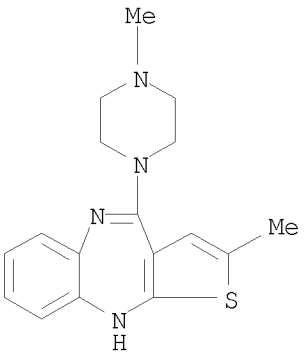
I

AB A process for the preparation of title compound I was disclosed. For example, a solution of 2-(2-aminoanilino)-5-methylthiophene-3-carbonitrile (10.0 g), N-methylpiperazine (60 mL) and N-methylpiperazine hydrochloride (24 gm) was heated at 120 °C until the reaction was completed to afford after work olanzapine. Of note, 2-polymorphic forms of olanzapine were isolated.

IT 132539-06-1P, Olanzapine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polymorphic forms I, II; preparation of olanzapine)

RN 132539-06-1 CAPLUS

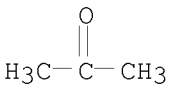
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



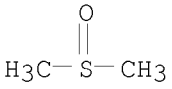
IT 67-64-1, Acetone, uses 67-68-5, Dimethyl sulfoxide, uses 68-12-2, Dimethylformamide, uses 71-36-3, n-Butanol, uses 75-05-8, Acetonitrile, uses 108-88-3, Toluene, uses 109-99-9, Tetrahydrofuran, uses 141-78-6, Ethyl acetate, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of olanzapine)

RN 67-64-1 CAPLUS

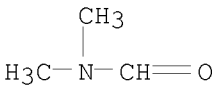
CN 2-Propanone (CA INDEX NAME)



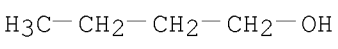
RN 67-68-5 CAPLUS
CN Methane, 1,1'-sulfinylbis- (CA INDEX NAME)



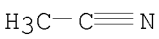
RN 68-12-2 CAPLUS
CN Formamide, N,N-dimethyl- (CA INDEX NAME)



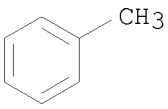
RN 71-36-3 CAPLUS
CN 1-Butanol (CA INDEX NAME)



RN 75-05-8 CAPLUS
CN Acetonitrile (CA INDEX NAME)



RN 108-88-3 CAPLUS
CN Benzene, methyl- (CA INDEX NAME)

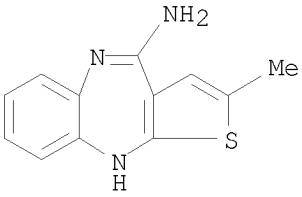


RN 109-99-9 CAPLUS
CN Furan, tetrahydro- (CA INDEX NAME)

RN 141-78-6 CAPLUS
CN Acetic acid ethyl ester (CA INDEX NAME)

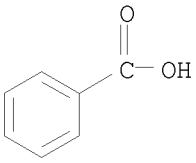
Et—O—Ac

IT 138564-60-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of olanzapine)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

IT 65-85-0, Benzoic acid, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of olanzapine)
RN 65-85-0 CAPLUS
CN Benzoic acid (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1200866 CAPLUS
DOCUMENT NUMBER: 143:452893
TITLE: Use of N-desmethylclozapine to treat human neuropsychiatric disease
INVENTOR(S): Weiner, David M.; Brann, Mark R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 38 pp., Cont.-in-part of U.S. Ser. No. 913,117.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050250767	A1	20051110	US 2005-98892	20050404
US 20040224942	A1	20041111	US 2004-761787	20040121
EP 1994932	A1	20081126	EP 2008-16004	20040121
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR				
US 20050085463	A1	20050421	US 2004-913117	20040805
AU 2005271513	A2	20060216	AU 2005-271513	20050804
AU 2005271513	A1	20060216		
CA 2576153	A1	20060216	CA 2005-2576153	20050804
WO 2006017614	A1	20060216	WO 2005-US27645	20050804
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1778244	A1	20070502	EP 2005-802835	20050804
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 101094674	A	20071226	CN 2005-80033997	20050804
JP 2008509147	T	20080327	JP 2007-524968	20050804
US 20060194831	A1	20060831	US 2006-416565	20060503
US 20060199807	A1	20060907	US 2006-417069	20060503
US 20070275957	A1	20071129	US 2007-671405	20070205

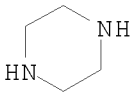
PRIORITY APPLN. INFO.:		
US 2003-442690P	P	20030123
US 2004-761787	A2	20040121
US 2004-913117	A2	20040805
EP 2004-704073	A3	20040121
US 2004-617553P	P	20041008
US 2005-98892	A	20050404
WO 2005-US27645	W	20050804

AB Disclosed herein is a method to treat neuropsychiatric diseases including psychosis, affective disorders, dementia, neuropathic pain, and glaucoma. Treatment is carried out by administering a therapeutically effective amount

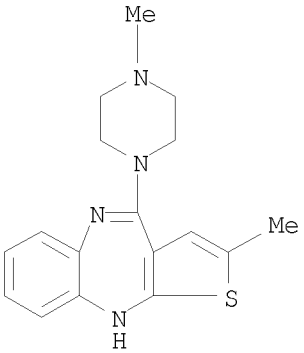
of N-desmethylclozapine to a patient suffering from a neuropsychiatric disease.

IT 110-85-0, Piperazine, biological studies 132539-06-1 , Olanzapine 161696-76-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of desmethylclozapine to treat human neuropsychiatric disease)

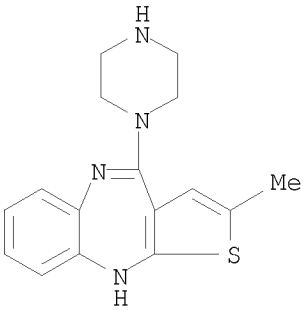
RN 110-85-0 CAPLUS
CN Piperazine (CA INDEX NAME)



RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



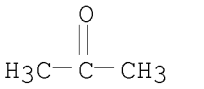
L29 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1042253 CAPLUS
DOCUMENT NUMBER: 143:332562
TITLE: Synthesis of 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine (olanzapine) and salts
INVENTOR(S): Mesar, Tomaz; Copar, Anton; Sturm, Hubert; Ludescher, Johannes
PATENT ASSIGNEE(S): Lek Pharmaceuticals D.D., Slovenia
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005090359	A2	20050929	WO 2005-EP2876	20050317
WO 2005090359	A3	20070426		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA				
SI 21747	A	20051031	SI 2004-79	20040318
AU 2005223338	A1	20050929	AU 2005-223338	20050317
CA 2558654	A1	20050929	CA 2005-2558654	20050317
EP 1749010	A2	20070207	EP 2005-716177	20050317
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
BR 2005007584	A	20070703	BR 2005-7584	20050317
CN 101084222	A	20071205	CN 2005-80015935	20050317
IN 2006CN03389	A	20070615	IN 2006-CN3389	20060918
US 20080161557	A1	20080703	US 2006-598816	20061214

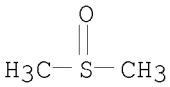
PRIORITY APPLN. INFO.:	SI 2004-79	A	20040318
	SI 2004-311	A	20041116
	WO 2005-EP2876	W	20050317

OTHER SOURCE(S): MARPAT 143:332562
AB The invention relates to a new process for the preparation of salts of olanzapine and transformation thereof into a pharmaceutically acceptable pure and discolored final product. The present invention also relates to new processes for the preparation of pure olanzapine. Thus, olanzapine was converted to its fumarate salt by reaction with fumaric acid in iso-PrOH.
IT 67-64-1, 2-Propanone, uses 67-68-5, uses 68-12-2, Dimethylformamide, uses 71-36-3, 1-Butanol, uses 75-05-8, Acetonitrile, uses 80-73-9 108-88-3, uses 109-60-4 109-99-9, uses 123-86-4, Butyl acetate 126-33-0 127-19-5 141-78-6, Acetic acid ethyl ester, uses 632-22-4

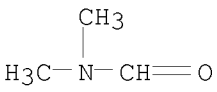
872-50-4, uses 1330-20-7, uses 7226-23-5
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of olanzapine and salts)
RN 67-64-1 CAPLUS
CN 2-Propanone (CA INDEX NAME)



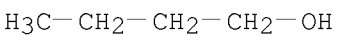
RN 67-68-5 CAPLUS
CN Methane, 1,1'-sulfinylbis- (CA INDEX NAME)



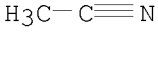
RN 68-12-2 CAPLUS
CN Formamide, N,N-dimethyl- (CA INDEX NAME)



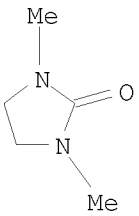
RN 71-36-3 CAPLUS
CN 1-Butanol (CA INDEX NAME)



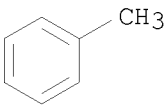
RN 75-05-8 CAPLUS
CN Acetonitrile (CA INDEX NAME)



RN 80-73-9 CAPLUS
CN 2-Imidazolidinone, 1,3-dimethyl- (CA INDEX NAME)



RN 108-88-3 CAPLUS
CN Benzene, methyl- (CA INDEX NAME)



RN 109-60-4 CAPLUS
CN Acetic acid, propyl ester (CA INDEX NAME)

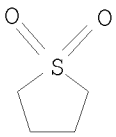
n-Pr—O—Ac

RN 109-99-9 CAPLUS
CN Furan, tetrahydro- (CA INDEX NAME)

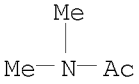
RN 123-86-4 CAPLUS
CN Acetic acid, butyl ester (CA INDEX NAME)

n-Bu—O—Ac

RN 126-33-0 CAPLUS
CN Thiophene, tetrahydro-, 1,1-dioxide (CA INDEX NAME)



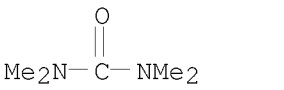
RN 127-19-5 CAPLUS
CN Acetamide, N,N-dimethyl- (CA INDEX NAME)



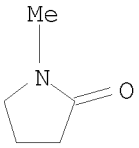
RN 141-78-6 CAPLUS
CN Acetic acid ethyl ester (CA INDEX NAME)

Et—O—Ac

RN 632-22-4 CAPLUS
CN Urea, N,N,N',N'-tetramethyl- (CA INDEX NAME)



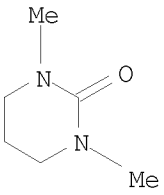
RN 872-50-4 CAPLUS
CN 2-Pyrrolidinone, 1-methyl- (CA INDEX NAME)



RN 1330-20-7 CAPLUS
CN Benzene, dimethyl- (CA INDEX NAME)

2 (D1—Me)

RN 7226-23-5 CAPLUS
CN 2(1H)-Pyrimidinone, tetrahydro-1,3-dimethyl- (CA INDEX NAME)

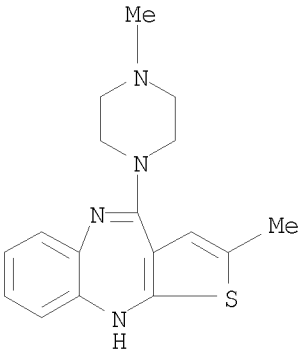


IT 777081-25-1P 861390-70-7P 865369-77-3P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of olanzapine and salts)
RN 777081-25-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine,

2-methyl-4-(4-methyl-1-piperazinyl)-, (2E)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

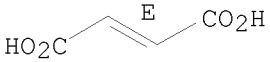
CRN 132539-06-1
CMF C17 H20 N4 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

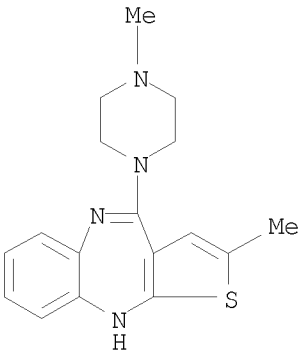
Double bond geometry as shown.



RN 861390-70-7 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-, benzoate (1:1) (CA INDEX NAME)

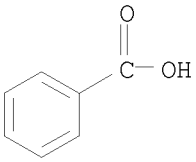
CM 1

CRN 132539-06-1
CMF C17 H20 N4 S



CM 2

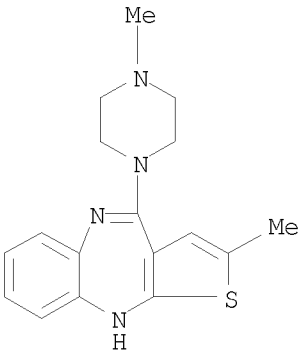
CRN 65-85-0
CMF C7 H6 O2



RN 865369-77-3 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-, ethanedioate (1:?) (CA INDEX NAME)

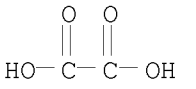
CM 1

CRN 132539-06-1
CMF C17 H20 N4 S

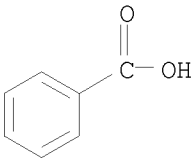


CM 2

CRN 144-62-7
CMF C2 H2 O4

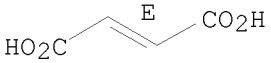


IT 65-85-0, Benzoic acid, reactions 110-17-8, Fumaric acid, reactions 110-85-0, Piperazine, reactions 144-62-7, Ethanedioic acid, reactions 138564-60-0, 4-Amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of olanzapine and salts)
RN 65-85-0 CAPLUS
CN Benzoic acid (CA INDEX NAME)

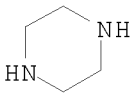


RN 110-17-8 CAPLUS
CN 2-Butenedioic acid (2E)- (CA INDEX NAME)

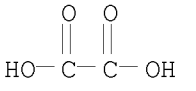
Double bond geometry as shown.



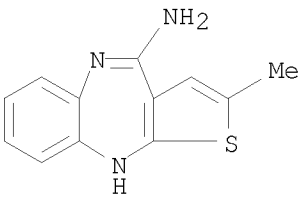
RN 110-85-0 CAPLUS
CN Piperazine (CA INDEX NAME)



RN 144-62-7 CAPLUS
CN Ethanedioic acid (CA INDEX NAME)

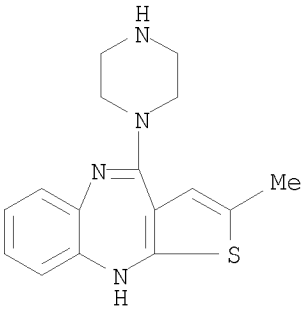


RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)

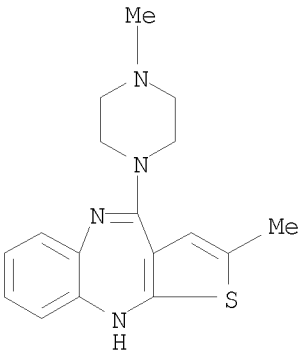


● HCl

IT 161696-76-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of olanzapine and salts)
RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



IT 132539-06-1P, Olanzapine
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of olanzapine and salts)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

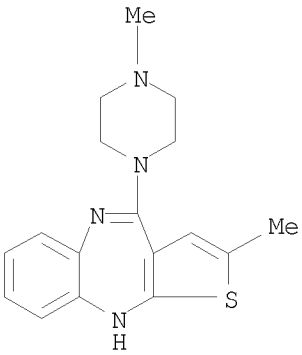


OS.CITING REF COUNT:	2	THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT:	4	THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

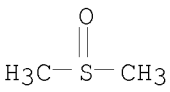
L29 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1004752 CAPLUS
DOCUMENT NUMBER: 143:311947
TITLE: Isopropanol water solvate of olanzapine
INVENTOR(S): Kotar-Jordan, Berta; Lenarsic, Roman; Grcman, Marija; Smrkolj, Matej; Meden, Anton; Simonic, Igor; Zupet, Rok; Gnidovec, Joze; Benkic, Primoz
PATENT ASSIGNEE(S): Krka, Tovarna Zdravil D.D. Novo Mesto, Slovenia
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005085256	A1	20050915	WO 2005-EP2389	20050307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
SI 21746	A	20051031	SI 2004-73	20040308
DE 102004060412	A1	20060706	DE 2004-102004060412	20041214
CA 2557986	A1	20050915	CA 2005-2557986	20050307
EP 1730153	A1	20061213	EP 2005-707723	20050307
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
NO 2006004484	A	20061129	NO 2006-4484	20061003
IN 2006CN03716	A	20070615	IN 2006-CN3716	20061009
US 20070191348	A1	20070816	US 2006-591831	20061023
PRIORITY APPLN. INFO.:			SI 2004-73 A	20040308
			DE 2004-102004060412A	20041214
			WO 2005-EP2389 W	20050307

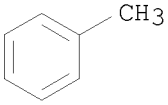
AB The invention relates to a novel and well defined solvate form of olanzapine which contains 2 mols. of water and 1 mol. of isopropanol per 2 mols. of olanzapine, and which can be converted into other, forms of olanzapine, in particular form I of olanzapine, as well as processes for preparing form I olanzapine.
IT 132539-06-1, Olanzapine
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(polymorphism; prepn of isopropanol water solvates of olanzapine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



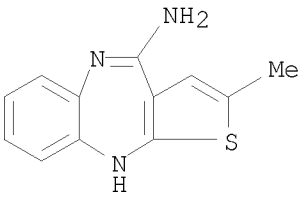
IT 67-68-5, Dimethylsulfoxide, uses 108-88-3, Toluene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(prepn of isopropanol water solvates of olanzapine)
RN 67-68-5 CAPLUS
CN Methane, 1,1'-sulfinylbis- (CA INDEX NAME)



RN 108-88-3 CAPLUS
CN Benzene, methyl- (CA INDEX NAME)

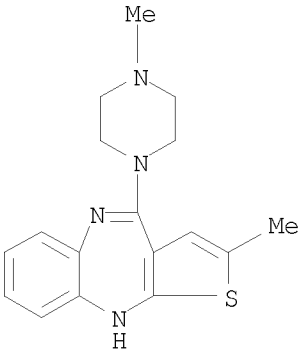


IT 138564-60-0, 4-Amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn of isopropanol water solvates of olanzapine)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



HCl

IT 132539-06-1DP, Olanzapine, methylene chloride hemisolvate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn of isopropanol water solvates of olanzapine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn of isopropanol water solvates of olanzapine
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:962265 CAPLUS
DOCUMENT NUMBER: 143:235359
TITLE: Process for the preparation of olanzapine form 1 useful as antipsychotic drug
INVENTOR(S): Rammohan Rao, Davuluri; Dwivedi, Shriprakash Dhar; Sreenivasulu, Pamujula; Sasi Kiran, Surapaneni
PATENT ASSIGNEE(S): Neuland Laboratories Limited, India
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

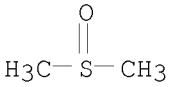
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005080401	A1	20050901	WO 2004-IN210	20040716
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2004CH00128	A	20060203	IN 2004-CH128	20040219
EP 1716154	A1	20061102	EP 2004-770670	20040716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
US 20070072845	A1	20070329	US 2005-557650	20051118
PRIORITY APPLN. INFO.:			IN 2004-CH128 A	20040219
			WO 2004-IN210 W	20040716

AB This invention provides an improved process for the preparation of Olanzapine Form (I). More specially, the invention provides in-situ improved process for the direct preparation of crystalline form of Olanzapine Form (I). The present invention also provides highly pure Olanzapine Form I with single individual impurity less than 0. 1 % by HPLC. The process comprises: (1) refluxing a mixture of 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride, N-methylpiperazine, DMSO,and toluene at 110-130°, (2) cooling the reaction mixture to 20-90°, (3) adding water to the cooled mixture, (4) cooling the resulting mixture to (-10)-30°, (5) filtering the mixture, (6) slurring the resulting wet cake with water at 50-90°, (7) filtering the material and sucking dry, (8) repeating the steps 6 to 7 till the traces of DMSO and its odor are removed, (9) dissolving the resulting wet cake in a chlorinated solvent at 25-30°, (10) separating the aqueous layer, (11) stirring the organic layer with anhydrous Na2SO4 or anhydrous MgSO4, (12) filtering and washing with CH2Cl2, (13) repeating the steps (11) and (12) till the moisture content is ≤ 0.1 %, and (14) purging dry ammonia gas in CH2Cl2 layer to get polymorphic form of Olanzapine form I. The process continues as follows; (15) removing the MgSO4 from the reaction mixture and washing the salts with CH2Cl2, (16) refluxing the CH2Cl2 layer, (17) concentrating the reaction mixture

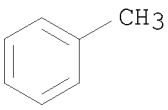
under vacuum, (18) cooling the reaction mixture to a temperature, (19) stirring the material at 0-5°, (20) filtering the material and washing with chilled CH2Cl2, (21) air drying the material, and (22) vacuum drying the product at 60-70°.

IT 67-68-5, DMSO, uses 108-88-3, Toluene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of olanzapine form 1 useful as antipsychotic drug)

RN 67-68-5 CAPLUS
CN Methane, 1,1'-sulfinylbis- (CA INDEX NAME)

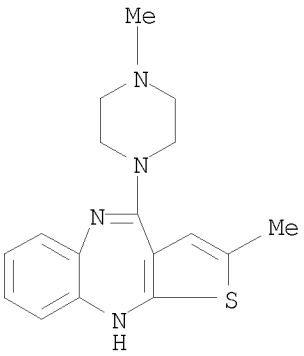


RN 108-88-3 CAPLUS
CN Benzene, methyl- (CA INDEX NAME)



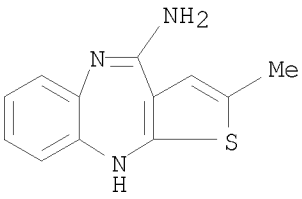
IT 132539-06-1P, Olanzapine
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of olanzapine form 1 useful as antipsychotic drug)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0, 4-Amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of olanzapine form 1 useful as antipsychotic drug)

RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:696918 CAPLUS
DOCUMENT NUMBER: 143:179518
TITLE: Preparation of stable salts of olanzapine
INVENTOR(S): Keltjens, Rolf
PATENT ASSIGNEE(S): Synthon B.V., Neth.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005070938	A1	20050804	WO 2005-EP835	20050126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1709053	A1	20061011	EP 2005-707055	20050126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
US 20050267099	A1	20051201	US 2005-50850	20050127
US 7329747	B2	20080212		
US 20050272721	A1	20051208	US 2005-50852	20050127
US 7459449	B2	20081202		

PRIORITY APPLN. INFO.:	US 2004-539120P	P	20040127
	US 2004-569607P	P	20040511
	WO 2005-EP835	W	20050126

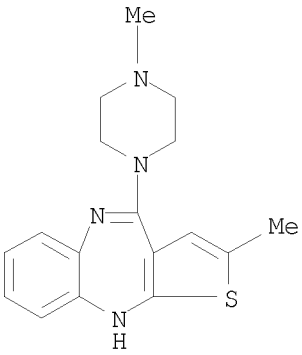
AB Several salts of olanzapine, including olanzapine malonate, olanzapine glycolate, olanzapine maleate, and olanzapine benzoate, have been found to have favorable solid state characteristics. To a clear solution of 5.0 g olanzapine base in 150 mL of acetone was added 1.67 g of malonic acid in 30 mL of acetone. The mixture was stirred at 40° for 3 h and the olanzapine hydrogenmalonate crystals were isolated by filtration, yield = 77%, m.p. 182-184°. Formulations of immediate-release tablets containing olanzapine are disclosed.

IT 861390-70-7P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of stable salts of olanzapine)

RN 861390-70-7 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-, benzoate (1:1) (CA INDEX NAME)

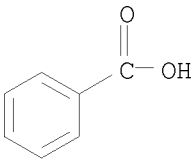
CM 1

CRN 132539-06-1
CMF C17 H20 N4 S

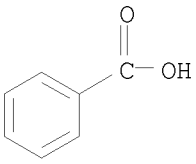


CM 2

CRN 65-85-0
CMF C7 H6 O2

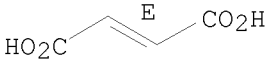


IT 65-85-0, Benzoic acid, reactions 110-17-8, Fumaric acid, reactions 132539-06-1, Olanzapine 161696-76-0, Desmethyl olanzapine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of stable salts of olanzapine)
RN 65-85-0 CAPLUS
CN Benzoic acid (CA INDEX NAME)

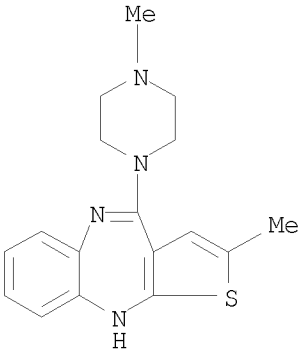


RN 110-17-8 CAPLUS
CN 2-Butenedioic acid (2E)- (CA INDEX NAME)

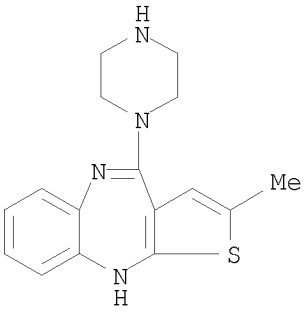
Double bond geometry as shown.



RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



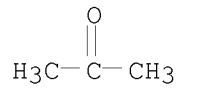
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:696917 CAPLUS
DOCUMENT NUMBER: 143:179517
TITLE: A process for making olanzapine in a polymorph form I
INVENTOR(S): Keltjens, Rolf
PATENT ASSIGNEE(S): Synthon B.V., Neth.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005070937	A1	20050804	WO 2005-EP834	20050126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1720885	A1	20061115	EP 2005-701231	20050126
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
US 20050272720	A1	20051208	US 2005-50851	20050127
PRIORITY APPLN. INFO.:			US 2004-539120P	P 20040127
			US 2004-562225P	P 20040415
			US 2004-569607P	P 20040511
			WO 2005-EP834	W 20050126

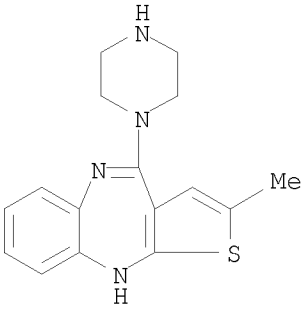
AB Heating a solid, preferably crystalline, olanzapine acetate produces olanzapine form I in high purity, free of other olanzapine forms and in good yields. The olanzapine acetate can also be used to purify raw or tech. grade olanzapine and to serve as an intermediary to other forms of olanzapine base. Olanzapine acetate was prepared by the reaction of olanzapine with acetic acid. Olanzapine acetate was stored at 65-70° for 18 h to obtain the olanzapine form I.

IT 67-64-1, Acetone, uses
RL: NUU (Other use, unclassified); USES (Uses)
(process for making olanzapine in polymorph form I)
RN 67-64-1 CAPLUS
CN 2-Propanone (CA INDEX NAME)

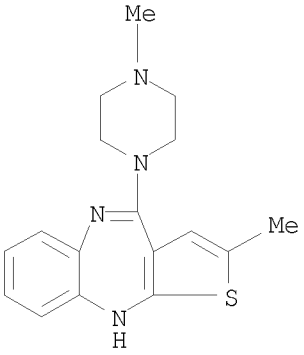


IT 161696-76-0, N-Demethyl olanzapine
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for making olanzapine in polymorph form I)

RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



IT 132539-06-1P, Olanzapine
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(process for making olanzapine in polymorph form I)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

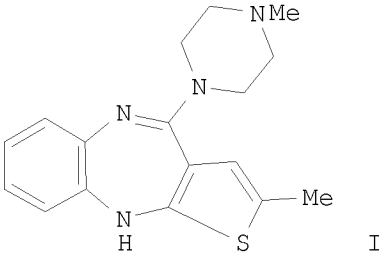


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

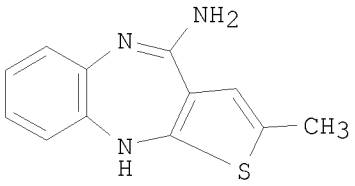
L29 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:596105 CAPLUS
DOCUMENT NUMBER: 143:115576
TITLE: Method for preparing olanzapine
INVENTOR(S): Cen, Junda; Zhong, Huijuan
PATENT ASSIGNEE(S): Lianyungang Haosen Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 5 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1420117	A	20030528	CN 2001-134868	20011116
PRIORITY APPLN. INFO.:			CN 2001-134868	20011116

OTHER SOURCE(S): CASREACT 143:115576
GI



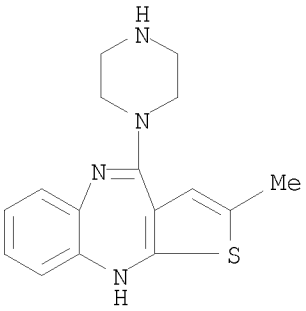
I



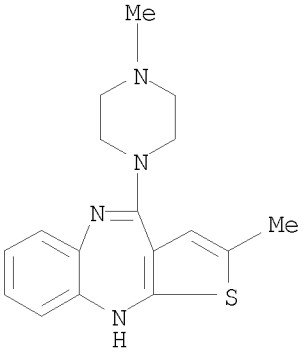
II

AB The invention is related to a scalable process for the preparation of olanzapine I, a psychotropic agent. Substitution of amine II·HCl with anhydrous piperazine in DMSO/toluene under refluxing for 12 h followed by N-methylation with HCHO/HCOOH in DMSO at 80°C for 2 h gave I in 68% yield. This efficient two-step process is better than the one-step one in which expensive N-methylpiperazine was used as starting material.

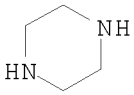
IT 161696-76-0P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of olanzapine via substitution of aminothienobenzodiazepine with piperazine followed by methylation with formaldehyde/formic acid)
RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



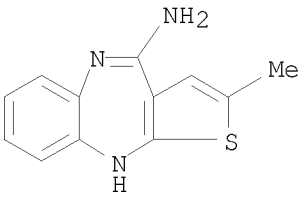
IT 132539-06-1P, Olanzapine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of olanzapine via substitution of aminothienobenzodiazepine with piperazine followed by methylation with formaldehyde/formic acid)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 110-85-0, Piperazine, reactions 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of olanzapine via substitution of aminothienobenzodiazepine with piperazine followed by methylation with formaldehyde/formic acid)
RN 110-85-0 CAPLUS
CN Piperazine (CA INDEX NAME)



RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

L29 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:349001 CAPLUS
DOCUMENT NUMBER: 142:386016
TITLE: Use of N-desmethylclozapine to treat human neuropsychiatric disease
INVENTOR(S): Weiner, David M.; Brann, Mark R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 34 pp., Cont.-in-part of U.S Ser. No. 761,787.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050085463	A1	20050421	US 2004-913117	20040805
US 20040224942	A1	20041111	US 2004-761787	20040121
EP 1994932	A1	20081126	EP 2008-16004	20040121
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR				
US 20050250767	A1	20051110	US 2005-98892	20050404
AU 2005271513	A2	20060216	AU 2005-271513	20050804
AU 2005271513	A1	20060216		
CA 2576153	A1	20060216	CA 2005-2576153	20050804
WO 2006017614	A1	20060216	WO 2005-US27645	20050804
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1778244	A1	20070502	EP 2005-802835	20050804
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 101094674	A	20071226	CN 2005-80033997	20050804
JP 2008509147	T	20080327	JP 2007-524968	20050804
US 20060194831	A1	20060831	US 2006-416565	20060503
US 20060199807	A1	20060907	US 2006-417069	20060503
US 20070275957	A1	20071129	US 2007-671405	20070205
IN 2007KN00526	A	20070706	IN 2007-KN526	20070213
US 20090018119	A1	20090115	US 2008-235526	20080922

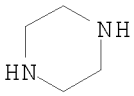
PRIORITY APPLN. INFO.:		
US 2003-442690P	P	20030123
US 2004-761787	A2	20040121
EP 2004-704073	A3	20040121
US 2004-913117	A2	20040805
US 2004-617553P	P	20041008
US 2005-98892	A	20050404
WO 2005-US27645	W	20050804

AB Disclosed herein is a method to treat neuropsychiatric diseases including

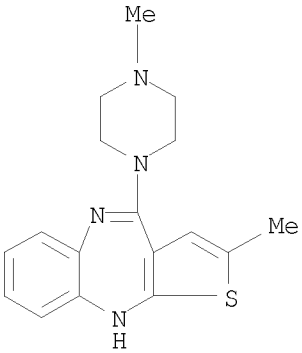
psychosis, affective disorders, dementia, neuropathic pain, and glaucoma. Treatment is carried out by administering a therapeutically effective amount of N-desmethylclozapine to a patient suffering from a neuropsychiatric disease.

IT 110-85-0, Piperazine, biological studies 132539-06-1 , Olanzapine 161696-76-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of N-desmethylclozapine to treat human neuropsychiatric disease)

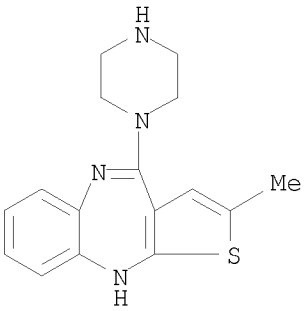
RN 110-85-0 CAPLUS
CN Piperazine (CA INDEX NAME)



RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)

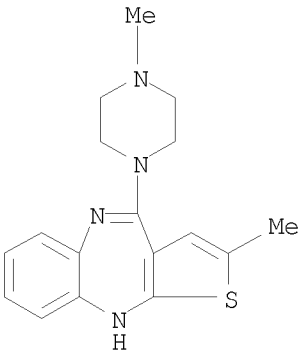


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

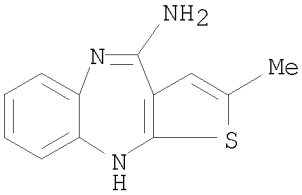
L29 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:203552 CAPLUS
DOCUMENT NUMBER: 140:253583
TITLE: Process of preparation of olanzapine form I
INVENTOR(S): Patel, Hiren V.; Ray, Anup K.; Patel, Pramod B.; Patel, Mahendra R.
PATENT ASSIGNEE(S): Sandoz, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp., Cont.-in-part of U.S. Ser. No. 160,958.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040048854	A1	20040311	US 2003-449643	20030530
US 7297789	B2	20071120		
US 20080188465	A1	20080807	US 2007-928791	20071030

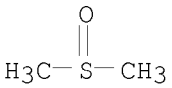
PRIORITY APPLN. INFO.: US 2002-160958 A2 20020531
US 2003-449643 A1 20030530
OTHER SOURCE(S): CASREACT 140:253583
AB Disclosed is a process for the preparation of polymorph form I of 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine (olanzapine) by reacting (a) reacting 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride and 1-methylpiperazine in an aprotic high boiling solvent or mixts. thereof at a temperature of between about 90 to 130°.; (b) purifying the product of step (a) in an acidic medium; (c) basifying the product of step (b) to a pH of between 7.5-9; and (d) extracting the product of step (c) using a low boiling organic solvent. Olanzapine is known as an antipsychotic agent and polymorph form I is in pharmaceutical formulations.
IT 132539-06-1P, Olanzapine
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process of preparation of olanzapine polymorph form I by reacting 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride and 1-methylpiperazine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



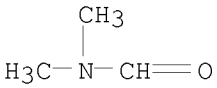
IT 138564-60-0, 4-Amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; process of preparation of olanzapine polymorph form I by reacting 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride and 1-methylpiperazine)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



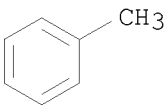
IT 67-68-5, Dimethyl sulfoxide, uses 68-12-2, Dimethylformamide, uses 108-88-3, Toluene, uses 141-78-6, Ethyl acetate, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; process of preparation of olanzapine polymorph form I by reacting 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride and 1-methylpiperazine)
RN 67-68-5 CAPLUS
CN Methane, 1,1'-sulfinylbis- (CA INDEX NAME)



RN 68-12-2 CAPLUS
CN Formamide, N,N-dimethyl- (CA INDEX NAME)



RN 108-88-3 CAPLUS
CN Benzene, methyl- (CA INDEX NAME)



RN 141-78-6 CAPLUS
CN Acetic acid ethyl ester (CA INDEX NAME)

Et—O—Ac

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L29 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:2889 CAPLUS
DOCUMENT NUMBER: 140:59669
TITLE: A process for the preparation of olanzapine by direct and reductive methylation of N-demethylolanzapine, and N-demethyl-N-formylolanzapine as an intermediate therefor
INVENTOR(S): Majka, Zbigniew; Stawinski, Tomasz; Rechnio, Justyna; Wieczorek, Maciej
PATENT ASSIGNEE(S): Adamed Sp. Z O.O., Pol.
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000847	A1	20031231	WO 2003-IB2181	20030610
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PL 199016	B1	20080829	PL 2002-354642	20020620
AU 2003240167	A1	20040106	AU 2003-240167	20030610
BR 2003005100	A	20040928	BR 2003-5100	20030610
EP 1513845	A1	20050316	EP 2003-732782	20030610
EP 1513845	B1	20070919		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1662543	A	20050831	CN 2003-814165	20030610
CN 100338069	C	20070919		
EP 1669359	A1	20060614	EP 2006-100356	20030610
EP 1669359	B1	20070829		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
AT 371660	T	20070915	AT 2006-100356	20030610
AT 373664	T	20071015	AT 2003-732782	20030610
ES 2289730	T3	20080201	ES 2006-100356	20030610
ES 2291644	T3	20080301	ES 2003-732782	20030610
NO 2004000658	A	20040213	NO 2004-658	20040213
HR 2004001075	B1	20080531	HR 2004-1075	20041117
MX 2004012200	A	20050826	MX 2004-12200	20041206

PRIORITY APPLN. INFO.:	PL 2002-354642	A	20020620
	EP 2003-732782	A3	20030610
	WO 2003-IB2181	W	20030610

OTHER SOURCE(S): CASREACT 140:59669
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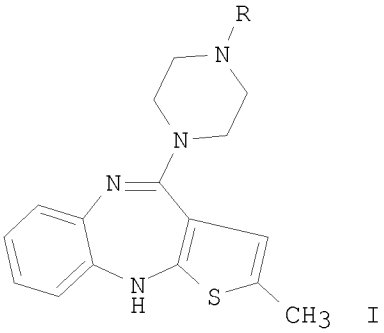


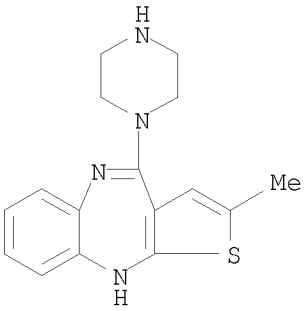
I

AB The invention relates to an improved process for the preparation of the CNS drug olanzapine, i.e., I [R = Me] (II). The process consists in N-methylation of N-demethylolanzapine, i.e., I [R = H] (III), which is also named 2-methyl-4-piperazin-1-yl-10H-thieno[2,3-b][1,5]benzodiazepine. The process utilizes several different reactions, including both reductive and direct methylation of III. Advantages of the invention include avoidance of hard-to-remove organic solvents, simpler chemical procedures, high yields, purity as good as the prior art, mild conditions, short reaction times, and low reaction temps. For instance, treatment of III with aqueous formalin in aqueous AcOH containing NaOAc at 0°, followed by treatment with NaBH4 at 0° under vigorous stirring, gave crude II of 97% purity by HPLC in 97.3% yield. Alternatively, direct methylation of III with MeI and K2CO3 in MeOH at room temperature gave II in 90% purity and 51% yield. The invention also relates to a new intermediate compound, N-demethyl-N-formylolanzapine, i.e., I [R = CHO] (IV), also named 2-methyl-4-(4-formyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine, and to a process for its preparation Thus, formylation of III with EtOCHO in refluxing THF gave 72.9% yield of IV, which was reduced with NaBH4 as above to give II in 88% purity and 86.9% yield. The starting material III was prepared in 85.7% yield by condensation of 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine HCl with piperazine in refluxing PhMe/DMSO mixture

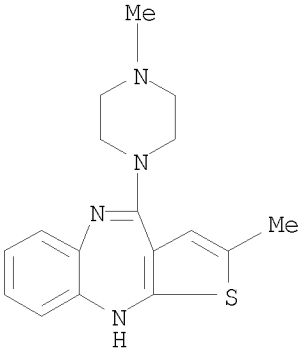
IT 161696-76-0P, N-Demethylolanzapine
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(improved preparation of olanzapine by methylation or reductive methylation of demethylolanzapine, or via reduction of formyldemethylolanzapine)

RN 161696-76-0 CAPLUS

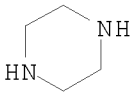
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



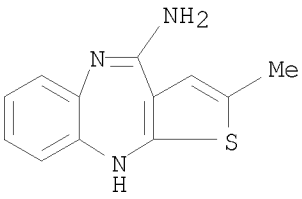
IT 132539-06-1P, Olanzapine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(improved preparation of olanzapine by methylation or reductive methylation of demethylolanzapine, or via reduction of formyldemethylolanzapine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 110-85-0, Piperazine, reactions 138564-60-0, 4-Amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(precursor; improved preparation of olanzapine by methylation or reductive methylation of demethylolanzapine, or via reduction of formyldemethylolanzapine)
RN 110-85-0 CAPLUS
CN Piperazine (CA INDEX NAME)



RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

OS.CITING REF COUNT:	2	THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT:	2	THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:532342 CAPLUS
DOCUMENT NUMBER: 139:95476
TITLE: Agents having serotonin-related pharmacol. activity for the pharmacological treatment of sleep apnea and other sleep-related breathing disorders
INVENTOR(S): Radulovacki, Miodrag; Carley, David W.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U.S. Ser. No. 16,901.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030130266	A1	20030710	US 2002-285277	20021031
US 7160898	B2	20070109		
US 20020086870	A1	20020704	US 2001-16901	20011214
US 6727242	B2	20040427		
CA 2503718	A1	20040521	CA 2003-2503718	20031029
CA 2503718	C	20090714		
WO 2004041272	A2	20040521	WO 2003-US34592	20031029
WO 2004041272	A3	20040916		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003301824	A1	20040607	AU 2003-301824	20031029
AU 2003301824	B2	20080904		
EP 1572202	A2	20050914	EP 2003-810822	20031029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015846	A	20050927	BR 2003-15846	20031029
CN 1708302	A	20051214	CN 2003-80102535	20031029
JP 2006511502	T	20060406	JP 2004-550292	20031029
NZ 539602	A	20070531	NZ 2003-539602	20031029
NO 2005002420	A	20050623	NO 2005-2420	20050519
IN 2005CN01058	A	20070727	IN 2005-CN1058	20050527
US 20060241164	A1	20061026	US 2006-404280	20060414
US 20070123517	A1	20070531	US 2006-643238	20061221
IN 2007CN05012	A	20080627	IN 2007-CN5012	20071106
US 20090005357	A1	20090101	US 2008-208482	20080911
US 20090221658	A1	20090903	US 2009-465186	20090513

PRIORITY APPLN. INFO.:

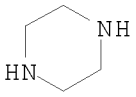
US 2001-16901	A2	20011214
US 1998-76216P	P	19980227
WO 1999-US4347	W	19990226
US 2000-622823	A1	20000823
US 2002-285277	A	20021031

WO 2003-US34592	W	20031029
US 2005-672168P	P	20050415
IN 2005-CN1058	A3	20050527
US 2006-404280	A3	20060414
US 2006-643238	B1	20061221

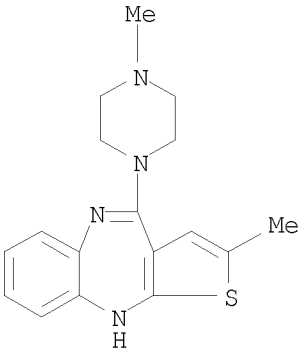
AB The invention discloses pharmacol. methods for the prevention of amelioration of sleep-related breathing disorders via administration of agents or combinations of agents that possess serotonin-related pharmacol. activity. Agents of the invention include e.g. ondansetron.

IT 110-85-0D, Piperazine, quaternized 132539-06-1, Olanzapine 132539-06-1D, Olanzapine, quaternized 161696-76-0 161696-76-0D, quaternized
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agents with serotonin-related pharmacol. activity for treatment of sleep apnea and other sleep-related breathing disorders)

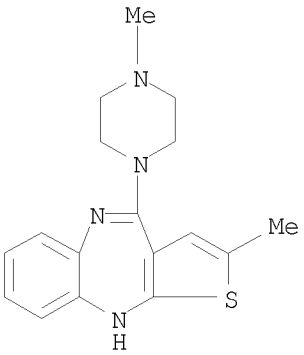
RN 110-85-0 CAPLUS
CN Piperazine (CA INDEX NAME)



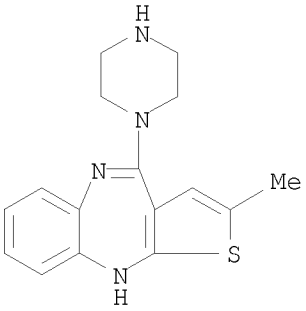
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



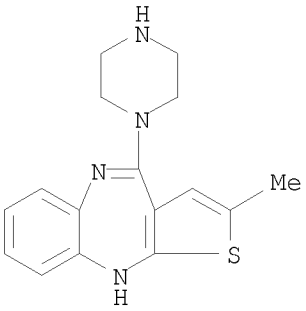
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:171904 CAPLUS
DOCUMENT NUMBER: 136:221739
TITLE: Process for preparation of hydrates of olanzapine and their conversion into crystalline forms of olanzapine
INVENTOR(S): Koprowski, Robert; Reguri, Buchi Reddy; Chakka, Ramesh
PATENT ASSIGNEE(S): Reddy's Laboratories Ltd., India
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

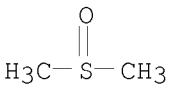
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018390	A1	20020307	WO 2001-US7258	20010307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IN 190895	A1	20030830	IN 2000-MA711	20000831
IN 191714	A1	20031220	IN 2000-MA709	20000831
CA 2420987	A1	20020307	CA 2001-2420987	20010307
AU 2001043475	A	20020313	AU 2001-43475	20010307
EP 1313742	A1	20030528	EP 2001-916449	20010307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014031	A	20030909	BR 2001-14031	20010307
HU 2003000875	A2	20031229	HU 2003-875	20010307
HU 2003000875	A3	20050928		
JP 2004507548	T	20040311	JP 2002-523905	20010307
NO 2003000926	A	20030424	NO 2003-926	20030227
ZA 2003001640	A	20040203	ZA 2003-1640	20030227
MX 2003001827	A	20041101	MX 2003-1827	20030228
US 20040067936	A1	20040408	US 2003-363436	20031120

PRIORITY APPLN. INFO.:			
IN 2000-MA709	A	20000831	
IN 2000-MA711	A	20000831	
WO 2001-US7258	W	20010307	

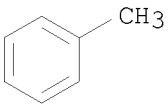
AB The present invention relates to a method for the preparation of hydrates of olanzapine. The present invention also relates to a process for conversion of these hydrates into a pure crystalline form of olanzapine referred to as form-1. The present invention also relates to a method of converting olanzapine form-2 to form-1. Thus, a mixture of 4-amino-2-methyl-10H-thieno-[2,3-b][1,5]benzodiazepine-HCl, N-methylpiperazine, DMSO, and toluene was heated under reflux, the mixture was cooled, and water was added. The olanzapine that was separated was dried to give a product with a moisture content of 5.22%.

IT 67-68-5, DMSO, uses 108-88-3, Toluene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of hydrates of olanzapine and their conversion into crystalline forms of olanzapine)

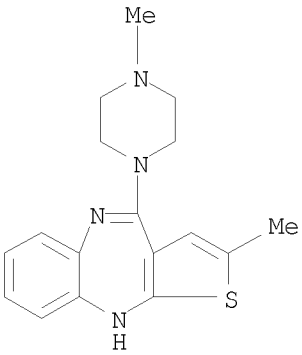
RN 67-68-5 CAPLUS
CN Methane, 1,1'-sulfinylbis- (CA INDEX NAME)



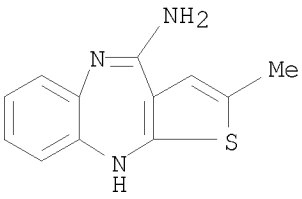
RN 108-88-3 CAPLUS
CN Benzene, methyl- (CA INDEX NAME)



IT 132539-06-1P, Olanzapine
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hydrates of olanzapine and their conversion into crystalline forms of olanzapine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



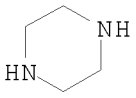
IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of hydrates of olanzapine and their conversion into crystalline forms of olanzapine)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



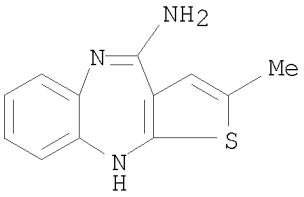
● HCl

OS.CITING REF COUNT:	12	THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)
REFERENCE COUNT:	3	THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:807597 CAPLUS
DOCUMENT NUMBER: 137:125141
TITLE: Synthesis of olanzapine
AUTHOR(S): Cen, Junda
CORPORATE SOURCE: Shanghai Institute of Pharmaceutical Industry, Shanghai, 200437, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2001), 32(9), 391-393
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 137:125141
AB Olanzapine was synthesized by condensation of S, propionaldehyde, and malononitrile in the presence of triethylamine to give 2-amino-5-methylthiophene-3-carbonitrile, condensation with 2-chloronitrobenzene in DMF in the presence of LiOH, reduction and ring-closure with SnCl2 to give 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine, condensation with piperazine, and methylation with HCOOH and HCHO in DMSO in an overall yield of 29%.
IT 110-85-0, Piperazine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of olanzapine)
RN 110-85-0 CAPLUS
CN Piperazine (CA INDEX NAME)

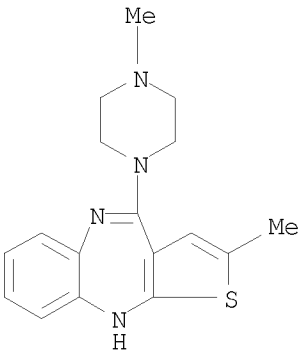


IT 138564-60-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of olanzapine)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



IT 132539-06-1P, Olanzapine
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of olanzapine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-
(CA INDEX NAME)



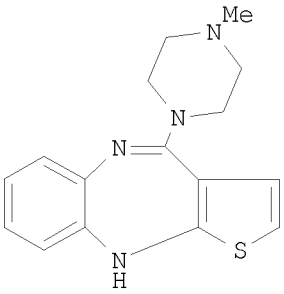
L29 ANSWER 26 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:324780 CAPLUS
DOCUMENT NUMBER: 127:5106
ORIGINAL REFERENCE NO.: 127:1161a,1164a
TITLE: Preparation of 2-methylthienobenzodiazepine as central nervous system agent.
INVENTOR(S): Chakrabarti, Jiban K.; Hotten, Terrence M.; Tupper, David E.
PATENT ASSIGNEE(S): Lilly Industries Ltd., UK
SOURCE: U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 44,844, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5627178	A	19970506	US 1995-387997	19950213
US 5229382	A	19930720	US 1992-890348	19920522
US 5817655	A	19981006	US 1996-748292	19961113
US 6008216	A	19991228	US 1998-122294	19980724
US 40033	E1	20080122	US 2001-23132	20011218

PRIORITY APPLN. INFO.:

US 1991-690143	B1	19910423
US 1992-890348	A2	19920522
US 1993-44844	B2	19930408
GB 1990-9229	A	19900425
US 1995-387997	A2	19950213
US 1996-748292	A3	19961113
US 1998-122294	E	19980724

GI

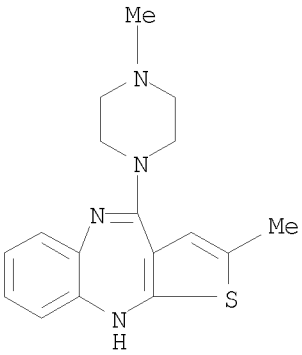


I

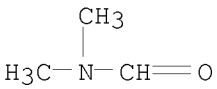
AB 2-Methyl-4-(4-methyl-1-piperazinyl)-10H-thieno-[2,3-b][1,5]benzodiazepine (I), or an acid salt thereof, has pharmaceutical properties, and is of particular use in the treatment of disorders of the central nervous system. Compound I is used in the treatment of schizophrenia, catatonic, delusional disorder, brief reactive psychosis, manic depression, anxiety disorder, post-traumatic stress disorder, obsessive compulsive disorder, delusions, hallucinations, and disorganized behavior. Thus, 4.3g of 4-amino-2-methyl-10H-thieno[2,3-b]benzodiazepine hydrochloride (preparation

given) was reluxed in a mixture of 15 mL of N-methylpiperazine, DMSO, and toluene for 20 h to give 1.65g I. Formulations containing I were described.

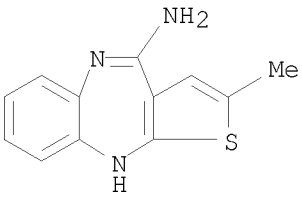
IT 132539-06-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-methyl-thieno-benzodiazepine as central nervous system agent)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 68-12-2, Dimethylformamide, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-methyl-thieno-benzodiazepine as central nervous system agent)
RN 68-12-2 CAPLUS
CN Formamide, N,N-dimethyl- (CA INDEX NAME)



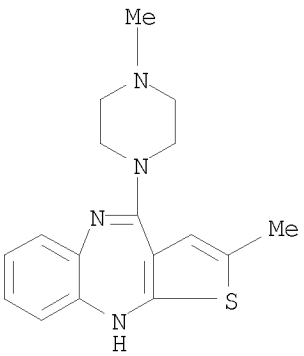
IT 138564-60-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-methyl-thieno-benzodiazepine as central nervous system agent)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



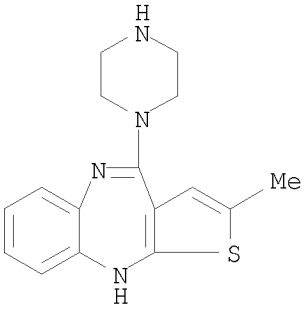
● HCl

OS.CITING REF COUNT:	7	THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT:	3	THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

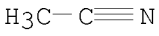
L29 ANSWER 27 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:383592 CAPLUS
DOCUMENT NUMBER: 122:197139
ORIGINAL REFERENCE NO.: 122:35861a,35864a
TITLE: Comparison of theory-based and empirical modeling for the prediction of chromatographic behavior in the ion-pairing separation of benzodiazepine-derived pharmaceutical compounds
AUTHOR(S): Larew, Larry A.; Olsen, Bernard A.; Stafford, John D.; Wilhelm, Melinda V.
CORPORATE SOURCE: Lilly Research Laboratories, Eli Lilly and Company, Lafayette, IN, 47902, USA
SOURCE: Journal of Chromatography, A (1995), 692(1 + 2), 183-93
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two approaches were examined for predicting chromatog. behavior during the reversed-phase ion-pairing separation of benzodiazepine-derived pharmaceutical compds. The capacity factor for olanzapine and its resolution from a closely related compound, desmethylolanzapine, were studied as a function of the percentage of acetonitrile, the ion-pairing reagent concentration and the buffer pH. In the first approach, the results were analyzed using the theory-based software package DryLab I/mp. In the second approach, statistical anal. was used to derive empirical equations to predict the dependence of the chromatog. behavior on each of the exptl. variables. At the lowest ion-pairing reagent concentration, DryLab I/mp was found to be a poor predictor of resolution For this complex separation, the empirical equations derived from the statistical anal. were found to predict better the chromatog. behavior over the ranges tested. These equations were used to generate response-surface plots to evaluate the method ruggedness.
IT 132539-06-1, Olanzapine 161696-76-0
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(modeling of chromatog. behavior in ion-pairing separation of benzodiazepine derivs.)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



IT 75-05-8, Acetonitrile, uses
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(modeling of chromatog. behavior in ion-pairing separation of benzodiazepine derivs.)
RN 75-05-8 CAPLUS
CN Acetonitrile (CA INDEX NAME)

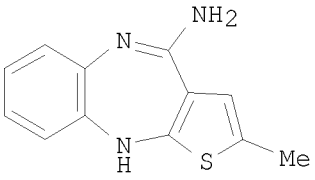


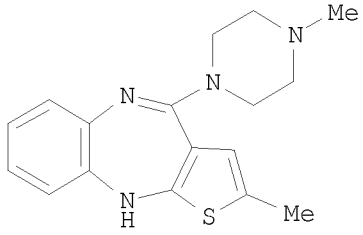
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

L31 ANSWER 1 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1538502 CAPLUS
DOCUMENT NUMBER: 150:35410
TITLE: Preparation of 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine and olanzapine
INVENTOR(S): Wieczorek, Maciej; Stawinski, Tomasz; Rechnio, Justyna
PATENT ASSIGNEE(S): Adamed Sp. z o.o., Pol.
SOURCE: Pol., 6pp.
CODEN: POXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Polish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PL 197478	B1	20080430	PL 2001-350717	20011116
PRIORITY APPLN. INFO.:			PL 2001-350717	20011116

OTHER SOURCE(S): CASREACT 150:35410
GI

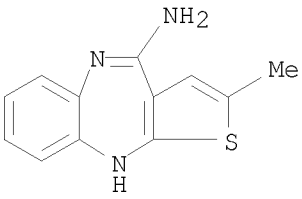

I


II

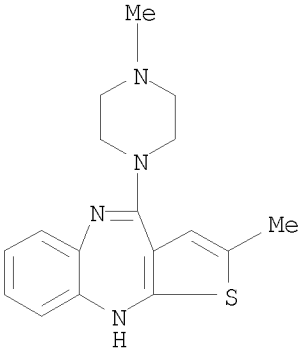
AB The title compound I.HCl, useful as an intermediate in the synthesis of olanzapine (II), was prepared by treating 2-(2-nitroanilino)-5-methylthiophene-3-carbonitrile with SnCl2 in the presence of aqueous NaOH followed by treatment of the free base with a solution of HCl in alc. Subsequently I.HCl was reacted with N-methylpiperazine to afford II.

IT 138564-60-0P, 4-Amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine and olanzapine)

RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



IT 132539-06-1P, Olanzapine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine and olanzapine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

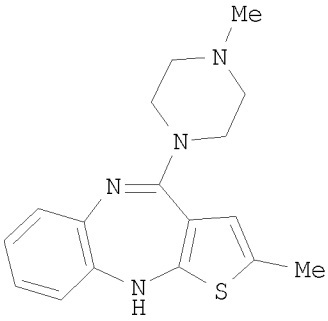


L31 ANSWER 2 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1536441 CAPLUS
DOCUMENT NUMBER: 150:77722
TITLE: Processes for the synthesis of olanzapine
INVENTOR(S): Kothakonda, Kiran Kumar; Che, Daqing; Guntoori, Bhaskar Reddy
PATENT ASSIGNEE(S): Apotex Pharmachem Inc., Can.
SOURCE: U.S. Pat. Appl. Publ., 4pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20080319189	A1	20081225	US 2007-976978	20071030
CA 2593407	A1	20081222	CA 2007-2593407	20070622
WO 2009000067	A1	20081231	WO 2008-CA1123	20080612

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: CA 2007-2593407 A 20070622
US 2007-976978 A 20071030
OTHER SOURCE(S): CASREACT 150:77722
GI



I

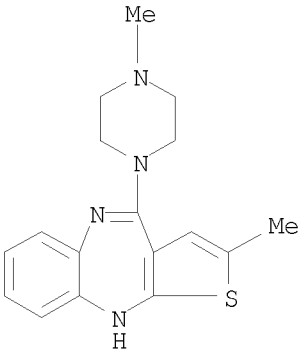
AB The invention provided a process for the preparation of olanzapine, I, in a C1-4 alc. solvent or a mixture of them. Compound I was prepared by condensation of 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine with

N-methylpiperazine in 1-propanol.

IT 132539-06-1P, Olanzapine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of olanzapine via condensation of amino(methyl)thienobenzodiazepine with methylpiperazine in low aliphatic alc.)

RN 132539-06-1 CAPLUS

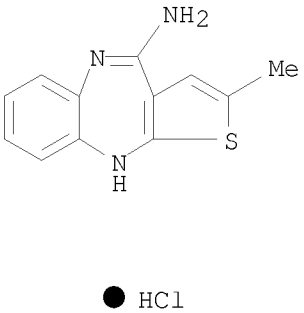
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of olanzapine via condensation of amino(methyl)thienobenzodiazepine with methylpiperazine in low aliphatic alc.)

RN 138564-60-0 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)

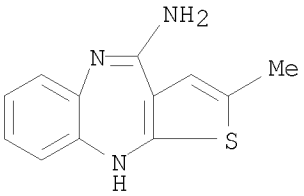


L31 ANSWER 3 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:181154 CAPLUS
DOCUMENT NUMBER: 146:365589
TITLE: A process for the preparation of olanzapine dihydrate
INVENTOR(S): Reguri, Buchi Reddy; Chakka, Ramesh
PATENT ASSIGNEE(S): Dr. Reddy's Laboratories, India
SOURCE: Indian Pat. Appl., 19pp.
CODEN: INXXBQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 2001MA00738	A	20050304	IN 2001-MA738	20010906
PRIORITY APPLN. INFO.:			IN 2001-MA738	20010906

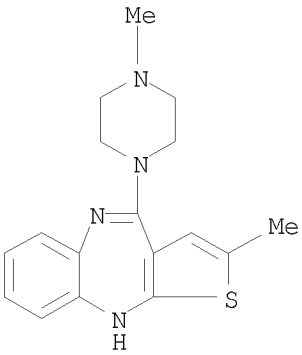
AB The present invention relates to a simple method for conversion of olanzapine dehydrate to olanzapine Form 1 by recrystn. of olanzapine dihydrate in dichloromethane. The process adopted herein is com. viable and well suited for industrial scale up. Olanzapine dihydrate was prepared by the reaction of olanzamine with N-methylpiperazine and the product was characterized by x-ray crystallog.

IT 138564-60-0, Olanzamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of olanzapine dihydrate)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

IT 132539-06-1, Olanzapine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(process for preparation of olanzapine dihydrate)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)


Me
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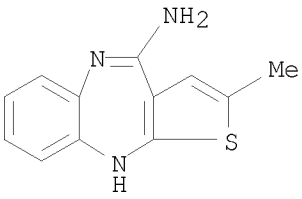
L31 ANSWER 4 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:215328 CAPLUS
DOCUMENT NUMBER: 144:280623
TITLE: A process for the preparation of anhydrous olanzapine hydrochloride of Form-1
INVENTOR(S): Alla, Venkat Reddy; Vyakaranam, Kameswara Rao; Marella, Venugopala Reddy; Sirigiri, Aruna Kumari; Bodapati, Sreenivasa Reddy; Billa, Ranadheer Reddy
PATENT ASSIGNEE(S): Lee Pharma Private Limited, India
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006025065	A1	20060309	WO 2004-IN270	20040831
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
IN 2006CN01166	A	20060519	IN 2006-CN1166	20060405
PRIORITY APPLN. INFO.:			WO 2004-IN270 W	20040831

AB Malononitrile is treated with propionaldehyde in the presence of sulfur powder and triethylamine in DMF to give 5-amino-4-cyano-2-methylthiophene. 2-Fluoronitrobenzene is condensed with 5-amino-4-cyano-2-methylthiophene in isopropanol and KOH powder give 4-cyano-2-methyl-1-(2-nitrophenylamino)thiophene. Reduction of the thiophene derivative with SnCl2 and HCl in isopropanol followed by cyclization produces 4-amino-2-methyl-10H-thieno[2,3,-b][1,5]benzodiazepine . Condensation of the above thieno[2,3,-b][1,5]benzodiazepine derivative with N-methylpiperazine in DMSO and toluene gives olanzapine tech. grade in anhydrous form. Recrystn. of the tech. grade anhydrous olanzapine in CH2Cl2 gives anhydrous olanzapine-HCl Form-I.

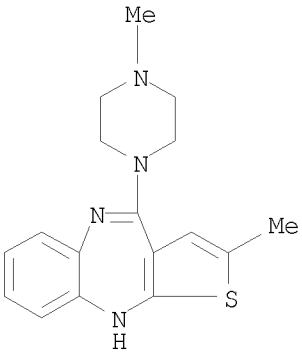
IT 138564-60-0P, 4-Amino-2-Methyl-10H-Thieno[2,3,-b][1,5]Benzodiazepine hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for the preparation of anhydrous olanzapine hydrochloride of form-1)

RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

IT 132539-06-1P, Olanzapine
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(process for the preparation of anhydrous olanzapine hydrochloride of form-1)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 5 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:101681 CAPLUS
DOCUMENT NUMBER: 144:177425
TITLE: Olanzapine salts and their conversion to olanzapine free base
INVENTOR(S): Simonic, Igor; Lenarsic, Roman; Kotar-Jordan, Berta; Zupet, Rok; Gnidovec, Joze
PATENT ASSIGNEE(S): Krka, Tovarna Zdravil, D.D., Novo Mesto, Slovenia
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

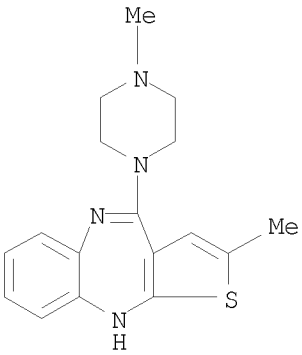
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006010620	A2	20060202	WO 2005-EP8218	20050728
WO 2006010620	A3	20060608		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
SI 21850	A	20060228	SI 2004-219	20040728
EP 1781665	A2	20070509	EP 2005-779020	20050728
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRIORITY APPLN. INFO.: SI 2004-219 A 20040728
WO 2005-EP8218 W 20050728

AB The present invention provides olanzapine salts useful as intermediates in the isolation of olanzapine from complex reaction mixts. These salts can be used for the production of olanzapine base which has a suitable purity for pharmaceutical use and can easily be converted to anhydrous olanzapine polymorphic form I, in high yields. Salts such as acetate, benzoate, dihydrochloride and solvates such as mixed water-isopropanol and dichloromethane were prepared

IT 132539-06-1P, Olanzapine 861390-70-7P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of olanzapine form I from olanzapine salts)

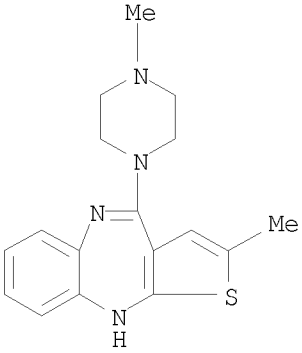
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 861390-70-7 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-, benzoate (1:1) (CA INDEX NAME)

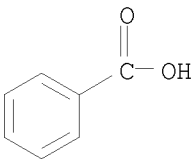
CM 1

CRN 132539-06-1
CMF C17 H20 N4 S



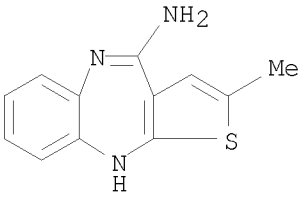
CM 2

CRN 65-85-0
CMF C7 H6 O2



IT 138564-60-0, 4-Amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)

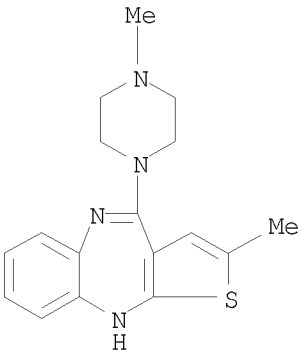
(preparation of olanzapine form I from olanzapine salts)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



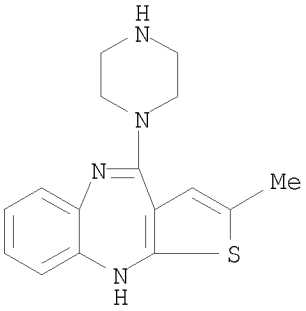
● HCl

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 6 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:3857 CAPLUS
DOCUMENT NUMBER: 145:201947
TITLE: General and independent approaches to predict HERG affinity values
AUTHOR(S): Fioravanzo, Elena; Cazzolla, Nicola; Durando, Lucia; Ferrari, Cristina; Mabilia, Massimo; Ombrato, Rosella; Parenti, Marco Daniele
CORPORATE SOURCE: S-IN Soluzioni Informatiche, Vicenza, 36100, Italy
SOURCE: Internet Electronic Journal of Molecular Design (2005), 4(9), 625-646
CODEN: IEJMAT; ISSN: 1538-6414
URL: ftp://biochempress.com/iejmd_2005_4_0625.pdf
PUBLISHER: BioChem Press
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The protein product of the human ether-a-go-go gene (hERG) is a potassium channel that when inhibited may lead to cardiac arrhythmia. At present, various in vivo and in vitro models for QT prolongation and subsequent arrhythmia exist but they may not be entirely predictive for humans. Consequently, a fast and reliable in silico model to assess hERG affinity values would increase the screening rate and would also lower the cost compared to exptl. assay methods. Several approaches were employed to predict hERG K+ channel affinities. Different QSAR models were developed employing various mol. descriptors. Independent software (EVA, DRAGON, LigPrep, PASS (Prediction of Activity Spectra for Substances), and QikProp) was used to predict hERG activity values. QikProp predicts pharmaceutically relevant properties for organic mols., starting from their 3D structures and employing calculated phys. significant descriptors. In addition to cell permeability, logP, solubility, blood/brain barrier permeability, the program can also predict hERG K+ channel affinity values. PASS PRO (Prediction of Activity Spectra for Substances), a program that can predict several hundred biol. activity probability values, such as pharmacol. effects, mechanisms of action, toxicity, and metabolism reactions, was trained to predict the probability of hERG activity. The availability of different and independent methods and models able to predict hERG activity allows the application of a consensus criterion to be used as a filter in the discovery process. Five QSAR models were obtained with Q2 values ranging from 0.65 to 0.98 and SDEP values ranging from 1.2 to 0.9. Employing QikProp, PASS, and QSAR predictions together, a consensus criterion was obtained that applied to 67 mols. yields a Matthews correlation coefficient (MCC) = 0.71, 5 false positives, and 3 false negatives. In the light of such result, our consensus score can be used as a powerful in silico screening for drug discovery processes.
IT 132539-06-1, Olanzapine 161696-76-0, Desmethylolanzapine
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(QSAR and software predictions of hERG potassium channel affinities of organic compds. and consensus criterion used for in silico screening for drug discovery processes)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

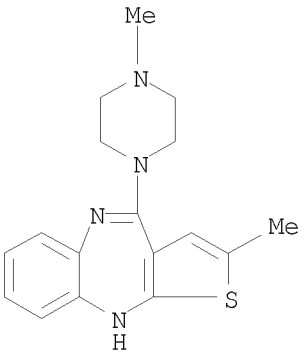


RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)

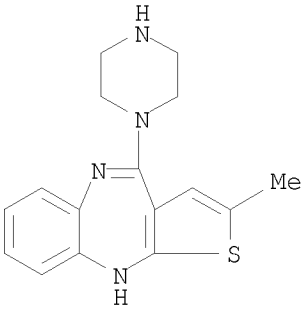


OS.CITING REF COUNT:	6	THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT:	12	THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 7 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1326877 CAPLUS
DOCUMENT NUMBER: 144:64260
TITLE: Intrinsic efficacy of antipsychotics at human D2, D3, and D4 dopamine receptors: Identification of the clozapine metabolite N-desmethylclozapine as a D2/D3 partial agonist
AUTHOR(S): Burstein, E. S.; Ma, J.; Wong, S.; Gao, Y.; Pham, E.; Knapp, A. E.; Nash, N. R.; Olsson, R.; Davis, R. E.; Hacksell, U.; Weiner, D. M.; Brann, M. R.
CORPORATE SOURCE: ACADIA Pharmaceuticals, San Diego, CA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2005), 315(3), 1278-1287
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Drugs that antagonize D2-like receptors are effective antipsychotics, but the debilitating movement disorder side effects associated with these drugs cannot be dissociated from dopamine receptor blockade. The "atypical" antipsychotics have a lower propensity to cause extrapyramidal symptoms (EPS), but the mol. basis for this is not fully understood nor is the impact of inverse agonism upon their clin. properties. Using a cell-based functional assay, we demonstrate that overexpression of Gαo induces constitutive activity in the human D2-like receptors (D2, D3, and D4). A large collection of typical and atypical antipsychotics was profiled for activity at these receptors. Virtually all were D2 and D3 inverse agonists, whereas none was D4 inverse agonist, although many were potent D4 antagonists. The inverse agonist activity of haloperidol at D2 and D3 receptors could be reversed by mesoridazine demonstrating that there were significant differences in the degrees of inverse agonism among the compds. tested. Aripiprazole and the principle active metabolite of clozapine NDMC [8-chloro-11-(1-piperazinyl)-5H-dibenzo [b,e] [1,4] diazepine] were identified as partial agonists at D2 and D3 receptors, although clozapine itself was an inverse agonist at these receptors. NDMC-induced functional responses could be reversed by clozapine. It is proposed that the low incidence of EPS associated with clozapine and aripiprazole used may be due, in part, to these partial agonist properties of NDMC and aripiprazole and that bypassing clozapine blockade through direct administration of NDMC to patients may provide superior antipsychotic efficacy.
IT 132539-06-1, Olanzapine 161696-76-0, N-Demethylolanzapine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intrinsic efficacy of antipsychotics at human D2, D3, and D4 dopamine receptors and identification of clozapine metabolite N-desmethylclozapine as D2/D3 partial agonist)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

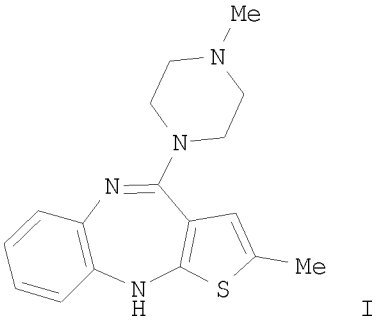


RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



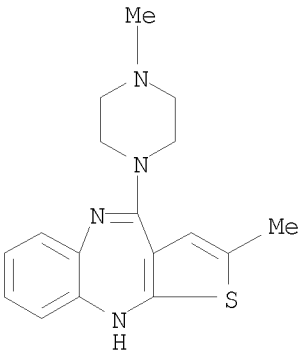
OS.CITING REF COUNT:	44	THERE ARE 44 CAPLUS RECORDS THAT CITE THIS RECORD (44 CITINGS)
REFERENCE COUNT:	41	THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 8 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:863646 CAPLUS
DOCUMENT NUMBER: 144:370058
TITLE: A Synthesis of tritium-labeled Olanzapine
AUTHOR(S): Shevchenko, V. P.; Nagaev, I. Yu.; Kuznetsov, Yu. V.; Polunin, E. V.; Zozulya, A. A.; Myasoedov, N. F.
CORPORATE SOURCE: Institute of Molecular Genetics, Russian Academy of Sciences, Moscow, 123182, Russia
SOURCE: Russian Journal of Bioorganic Chemistry (2005), 31(4), 378-382
CODEN: RJBCET; ISSN: 1068-1620
PUBLISHER: Pleiades Publishing, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:370058
GI

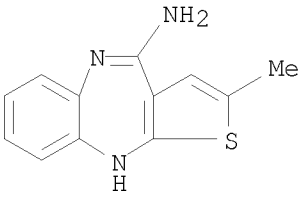


I

AB A synthesis of olanzapine (I), 2-methyl-10-(4-methyl-1-piperazinyl)-4H-thieno[2,3-b][1,5]benzodiazepine, was carried out and the conditions for its tritium labeling were optimized to obtain a tritium-labeled olanzapine preparation with a specific radioactivity of 12 Ci/mmol.
IT 132539-06-1P, Olanzapine 138564-60-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of olanzapine via Gewald heterocyclization of propionic aldehyde with malonodinitrile and sulfur followed by coupling with (fluoro)nitrobenzene, reduction with SnCl2-heterocyclization and condensation with (methyl)piperazine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

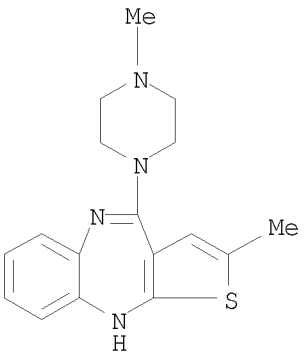
L31 ANSWER 9 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:813566 CAPLUS
DOCUMENT NUMBER: 144:218907
TITLE: Olanzapine form 1
AUTHOR(S): Anon.
CORPORATE SOURCE: Spain
SOURCE: IP.com Journal (2005), 5(6A), 34 (No. IPCOM000125182D), 23 May 2005
CODEN: IJPOBX; ISSN: 1533-0001
PUBLISHER: IP.com, Inc.
DOCUMENT TYPE: Journal; Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IP 125182D		20050523	IP 2005-125182D	20050523

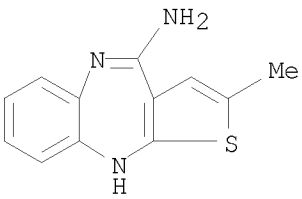
PRIORITY APPLN. INFO.: IP 2005-125182D 20050523

AB An improved method for the preparation of olanzapine form I is described. The method is based on the reaction of the benzodiazepine of formula II with methylpiperazine (III). The reaction is described in aprotic solvent such as toluene, dimethylsulfoxide or DMF. The obtained product is not pure and a crystallization is required to achieve the desired quality and polymorphic form.

IT 132539-06-1P, Olanzapine
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(improved synthesis and purification of olanzapine form I)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

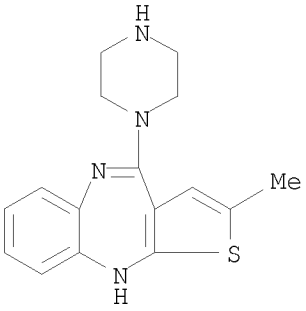


IT 138564-60-0, Olanzamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(improved synthesis and purification of olanzapine form I)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)

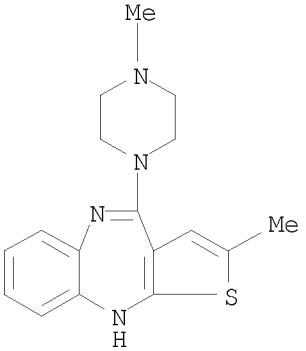


● HCl

L31 ANSWER 10 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:173373 CAPLUS
DOCUMENT NUMBER: 142:475224
TITLE: Low-Dose Fluvoxamine as an Adjunct to Reduce Olanzapine Therapeutic Dose Requirements: A Prospective Dose-Adjusted Drug Interaction Strategy
AUTHOR(S): Albers, Lawrence J.; Ozdemir, Vural; Marder, Stephen R.; Raggi, Maria Augusta; Aravagiri, Manickam; Endrenyi, Laszlo; Reist, Christopher
CORPORATE SOURCE: VA Long Beach Healthcare System and Department of Psychiatry and Human Behavior, College of Medicine, University of California, Irvine, CA, USA
SOURCE: Journal of Clinical Psychopharmacology (2005), 25(2), 170-174
CODEN: JCPYDR; ISSN: 0271-0749
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Despite the advances in antipsychotic pharmacotherapy over the past decade, many atypical antipsychotic agents are not readily accessible by patients with major psychosis or in developing countries where the acquisition costs may be prohibitive. Olanzapine is an efficacious and widely prescribed atypical antipsychotic agent. In theory, olanzapine therapeutic dose requirement may be reduced during concurrent treatment with inhibitors of drug metabolism In vitro studies suggest that smoking-inducible cytochrome P 450 (CYP) 1A2 contributes to formation of the metabolite 4'-N-desmethylolanzapine. The present prospective study tested the hypothesis that olanzapine steady-state doses can be significantly decreased by coadministration of a low subclin. dose of fluvoxamine, a potent inhibitor of cytochrome P 450 1A2. The study design followed a targeted "at-risk" population approach with a focus on smokers who were likely to exhibit increased cytochrome P 450 1A2 expression. Patients with stable psychotic illness (N = 10 men, all smokers) and receiving chronic olanzapine treatment were evaluated for steady-state plasma concns. of olanzapine and 4'-N-desmethylolanzapine. Subsequently, olanzapine dose was reduced from 17.5 ± 4.2 mg/d (mean ± SD) to 13.0 ± 3.3 mg/d, and a nontherapeutic dose of fluvoxamine (25 mg/d, PO) was added to regimen. Patients were reevaluated at 2, 4, and 6 wk during olanzapine-fluvoxamine cotreatment. There was no significant change in olanzapine plasma concentration, antipsychotic response, or metabolic indexes (eg, serum glucose and lipids) after dose reduction in the presence of fluvoxamine ($P > 0.05$). 4'-N-desmethylolanzapine/olanzapine metabolic ratio decreased from 0.45 ± 0.20 at baseline to 0.25 ± 0.11 at week 6, suggesting inhibition of the cytochrome P 450 1A2-mediated olanzapine 4'-N-demethylation by fluvoxamine ($P < 0.05$). In conclusion, this prospective pilot study suggests that a 26% reduction in olanzapine therapeutic dose requirement may be achieved by coadministration of a nontherapeutic oral dose of fluvoxamine.
IT 161696-76-0
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(4'-N-desmethylolanzapine/olanzapine ratio decreased after dose reduction in presence of fluvoxamine suggest inhibition of cytochrome P 450 1A2-mediated olanzapine 4'-N-desmethylation by fluvoxamine in psychosis patient)
RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



IT 132539-06-1, Olanzapine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(olanzapine in combination with fluvoxamine was well tolerated and coadministration of low dose of fluvoxamine as adjunct significantly decreased olanzapine therapeutic dose requirements in psychosis patient)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



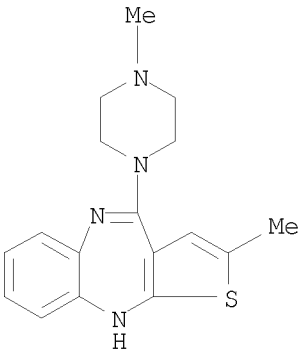
OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 11 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:41989 CAPLUS
DOCUMENT NUMBER: 142:424991
TITLE: Application of Accurate Mass Measurement to Urine Drug Screening
AUTHOR(S): Ojanperae, Ilkka; Pelander, Anna; Laks, Suvi; Gergov, Merja; Vuori, Erkki; Witt, Matthias
CORPORATE SOURCE: Department of Forensic Medicine, University of Helsinki, Helsinki, FIN-00014, Finland
SOURCE: Journal of Analytical Toxicology (2005), 29(1), 34-40
CODEN: JATOD3; ISSN: 0146-4760
PUBLISHER: Preston Publications
DOCUMENT TYPE: Journal
LANGUAGE: English

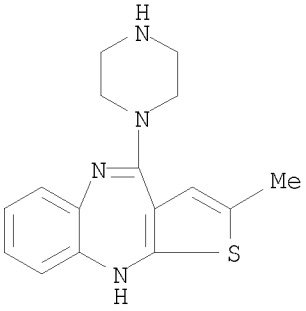
AB Poor availability of reference stds. for designer drugs, metabolites, and new substances prevents toxicol. labs. from rapidly responding to the changing anal. challenges of drug abuse. A novel screening approach comprising determination of accurate masses of sample components and comparison of these with databases of theor. monoisotopic masses is described. Using liquid chromatog.-time-of-flight mass spectrometry (LC-TOFMS), a routine mass search window of 20-30 ppm was applied to urine samples. The ultimate reference technique, liquid chromatog.-Fourier transform mass spectrometry (LC-FTMS), was capable of confirming the findings within a 3 ppm mass accuracy. Using a target database of 7640 compds., the number of potential elemental formulas ranged from one to three with LC-TOFMS, and it was always one with LC-FTMS. In contrast to ordinary techniques requiring primary reference stds., the formula-based databases can be updated instantly with fresh numeric data from scientific literature and authority sources. (c) 2005 Preston Publications.

IT 132539-06-1, Olanzapine 161696-76-0
RL: ANT (Analyte); ANST (Analytical study)
(urine drug screening by LC combined with TOF-MS or FT-MS)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



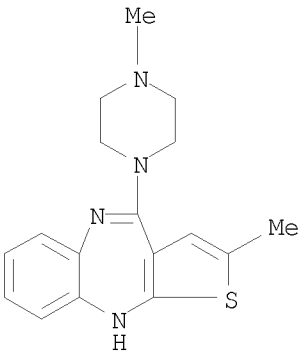
OS.CITING REF COUNT:	2	THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT:	35	THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 12 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:710561 CAPLUS
DOCUMENT NUMBER: 141:420004
TITLE: A study of matrix effects on an LC/MS/MS assay for olanzapine and desmethyl olanzapine
AUTHOR(S): Chin, C.; Zhang, Z. P.; Karnes, H. T.
CORPORATE SOURCE: PPD Development, Richmond, VA, 23230, USA
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2004), 35(5), 1149-1167
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

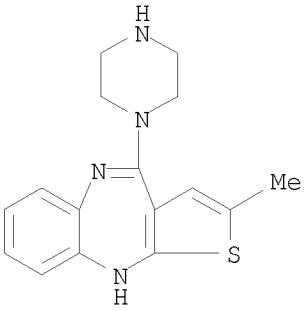
AB The purpose of this research project was to investigate potential matrix effects of anticoagulant and lipemia on the response of olanzapine, desmethylolanzapine, olanzapine-D3 and desmethylolanzapine-D8 in an LC/MS/MS assay. Blank human serum and sodium heparin, sodium citrate, and K3EDTA plasma with various degrees of lipemia were fortified with olanzapine, desmethyl olanzapine, olanzapine-D3 and desmethyl olanzapine-D8. Six replicates of each sample were extracted using Waters Oasis MCX cartridges and analyzed using electrospray LC/MS/MS. The analytes were separated on a Phenomenex LUNA Ph hexyl, 2 mm+50 mm, 5 μm, anal. column and a gradient rising from 2 to 85% mobile phase B. Mobile phase A consisted of acetonitrile-ammonium acetate (20 mM) (52:48 volume/volume) and mobile phase B was formic acid-acetonitrile (0.1:100 volume/volume). Ion suppression was investigated through post column infusion expts. The degree of lipemia of each sample, indicated by turbidity, was ranked into categories from least to greatest and used for statistical analyses. The results from anal. of variance testing indicated that lipemia, anticoagulant and their interaction significantly influenced mass spectral matrix effects and extraction matrix effects. Differential behavior between the analytes and labeled internal stds. contributed to variability. The most significant source of variability however, was ion suppression due to co-eluting matrix components.

IT 132539-06-1, Olanzapine 161696-76-0, Desmethylolanzapine
RL: ANT (Analyte); ANST (Analytical study)
(study of matrix effects on an LC/MS/MS assay for olanzapine and desmethylolanzapine and effects of anticoagulants and hyperlipidemia)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

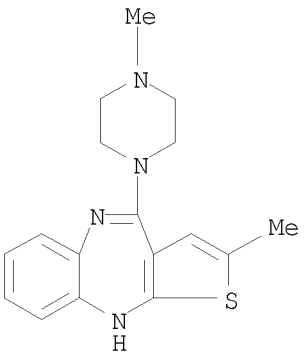


RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)

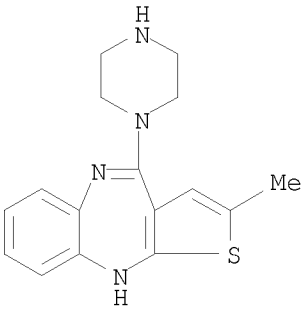


OS.CITING REF COUNT:	14	THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT:	30	THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 13 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:694160 CAPLUS
DOCUMENT NUMBER: 141:405400
TITLE: Evaluation of deuterium isotope effects in normal-phase LC-MS-MS separations using a molecular modeling approach
AUTHOR(S): Iyer, Sunil S.; Zhang, Zong-Ping; Kellogg, Glen E.; Karnes, H. Thomas
CORPORATE SOURCE: Department of Pharmaceutics, School of Pharmacy, Virginia Commonwealth University, Richmond, VA, 23298-0533, USA
SOURCE: Journal of Chromatographic Science (2004), 42(7), 383-387
CODEN: JCHSBZ; ISSN: 0021-9665
PUBLISHER: Preston Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mol. modeling of stationary phases presents a unique challenge because there is little available exptl. derived structural information. Verified interaction mechanisms at a mol. level with analytes are also rare. Mol. mechanics calcns. using the Tripos force field were carried out to qual. and quant. assess stationary phase interactions. Binding energy values of -15.40, 15.28, -12.53, and -12.34 kcal/mol, resp., were obtained for olanzapine (OLZ), OLZ-D3, des-Me olanzapine (DES), and DES-D8 that corresponded to the retention behavior of the four compds. observed using liquid chromatog.-mass spectrometry (MS)-MS. The model explains, semiquant., the deuterium isotope effect in the normal-phase chromatog. separation of these compds. (c) 2004 Preston Publications.
IT 132539-06-1, Olanzapine 161696-76-0
RL: ANT (Analyte); ANST (Analytical study)
(evaluation of deuterium isotope effects in normal-phase LC-MS-MS sepns. using a mol. modeling approach)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



OS.CITING REF COUNT:	4	THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT:	23	THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 14 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:633448 CAPLUS
DOCUMENT NUMBER: 141:167814
TITLE: Selective serotonin 2A/2C receptor inverse agonists as therapeutics for neurodegenerative diseases
INVENTOR(S): Weiner, David M.; Davis, Robert E.; Brann, Mark R.
PATENT ASSIGNEE(S): Acadia Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004064738	A2	20040805	WO 2004-US1234	20040115
WO 2004064738	A3	20041125		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
AU 2004206886	A1	20040805	AU 2004-206886	20040115
CA 2512639	A1	20040805	CA 2004-2512639	20040115
US 20040213816	A1	20041028	US 2004-759561	20040115
US 7601740	B2	20091013		
EP 1587789	A2	20051026	EP 2004-702584	20040115
EP 1587789	B1	20080903		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004006591	A	20051220	BR 2004-6591	20040115
JP 2006516284	T	20060629	JP 2006-501009	20040115
CN 1816524	A	20060809	CN 2004-80004479	20040115
RU 2332401	C2	20080827	RU 2005-125918	20040115
AT 407117	T	20080915	AT 2004-702584	20040115
EP 2009000	A1	20081231	EP 2008-15449	20040115
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR, AL, LT, LV, MK				
ES 2314362	T3	20090316	ES 2004-702584	20040115
NZ 541146	A	20090430	NZ 2004-541146	20040115
MX 2005007568	A	20050921	MX 2005-7568	20050714
ZA 2005005680	A	20060426	ZA 2005-5680	20050714
IN 2005KN01635	A	20060721	IN 2005-KN1635	20050816
US 20060199842	A1	20060907	US 2006-416594	20060503
US 20060264465	A1	20061123	US 2006-416527	20060503
US 20060264466	A1	20061123	US 2006-416855	20060503
IN 2007KN03282	A	20080104	IN 2007-KN3282	20070905

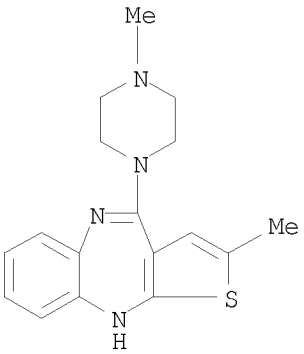
PRIORITY APPLN. INFO.:		
US 2003-441406P	P	20030116
US 2003-479346P	P	20030617
EP 2004-702584	A3	20040115
US 2004-759561	A1	20040115
WO 2004-US1234	W	20040115
IN 2005-KN1635	A3	20050816

AB Behavioral pharmacol. data with the compound of formula (I), a novel and selective 5HT2A/2C receptor inverse agonist, demonstrate in vivo efficacy in models of psychosis and dyskinesias. This includes activity in reversing MK-801 induced locomotor behaviors, suggesting that this compound

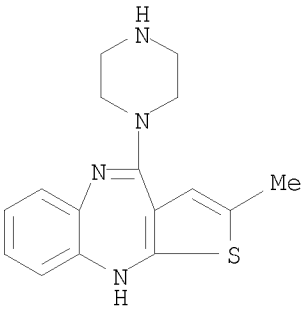
may be an efficacious anti-psychotic, and activity in an MPTP primate model of dyskinesias, suggesting efficacy as an anti-dyskinesia agent. These data support the hypothesis that 5HT2A/2C receptor inverse agonism may confer antipsychotic and anti-dyskinetic efficacy in humans, and indicate a use of the compound of formula (I) and related agents as novel therapeutics for Parkinson's Disease, related human neurodegenerative diseases, and psychosis.

IT 132539-06-1, Olanzapine 161696-76-0, N-Demethylolanzapine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serotonin 2A/2C receptor inverse agonists as therapeutics for neurodegenerative diseases)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)

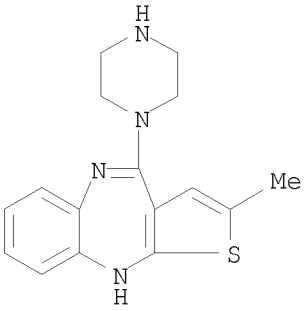


OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 15 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:498926 CAPLUS
DOCUMENT NUMBER: 141:98933
TITLE: Rapid analysis of olanzapine and desmethylolanzapine in human plasma using high-performance liquid chromatography with coulometric detection
AUTHOR(S): Sabbioni, Cesare; Saracino, Maria Addolorata; Mandrioli, Roberto; Albers, Lawrence; Boncompagni, Giancarlo; Raggi, Maria Augusta
CORPORATE SOURCE: Department of Pharmaceutical Sciences, Faculty of Pharmacy, Alma Mater Studiorum, University of Bologna, Bologna, 40126, Italy
SOURCE: Analytica Chimica Acta (2004), 516(1-2), 111-117
CODEN: ACACAM; ISSN: 0003-2670
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A rapid and sensitive liquid chromatog. method was developed for the simultaneous determination of olanzapine and its metabolite N-desmethylolanzapine in human plasma. A chromatog. run on a C8 (150 mm + 4.6 mm, 5 μm) column lasts about 8 min, using a mobile phase composed of methanol (30%) and a phosphate buffer (70%) of pH 3.5. A coulometric detector was used; the first coulometric cell was set at +350 mV and the second at -200 mV. A careful solid-phase extraction procedure,based on diol cartridges, was implemented for the pre-treatment of plasma samples; only 250 μL of plasma is needed for a complete anal. Linear responses were obtained between 0.4 and 40.0 ng mL-1 for both analytes, with a detection limit of 0.1 ng mL-1. Extraction yield values for the analytes exceeded 97%, with relative standard deviation <2.2%. Thus, precision was good; accuracy was also satisfactory. Due to its high selectivity and sensitivity, the proposed liquid chromatog. method seems to be suitable for therapeutic drug monitoring of patients treated with Zyprexa tablets undergoing polypharmacy and also for pharmacokinetic studies.

IT 161696-76-0
RL: ANT (Analyte); ANST (Analytical study)
(rapid anal. of olanzapine and desmethylolanzapine in human plasma using high-performance liquid chromatog. with coulometric detection)
RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)

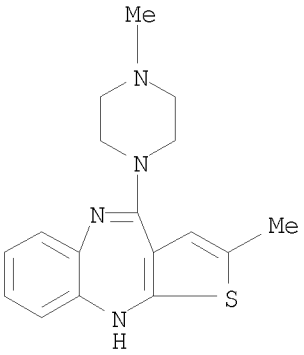


IT 132539-06-1, Olanzapine

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(rapid anal. of olanzapine and desmethylolanzapine in human plasma using high-performance liquid chromatog. with coulometric detection)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



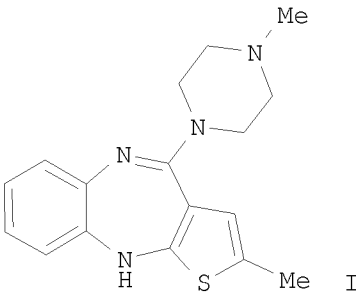
OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 16 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:972083 CAPLUS
DOCUMENT NUMBER: 140:16753
TITLE: Process of preparation of olanzapine form I
INVENTOR(S): Patel, Hiren V.; Ray, Anup K.; Patel, Pramod B.; Patel, Mahendra R.
PATENT ASSIGNEE(S): Geneva Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003101997	A1	20031211	WO 2003-US17186	20030530
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003237305	A1	20031219	AU 2003-237305	20030530
EP 1513846	A1	20050316	EP 2003-736771	20030530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

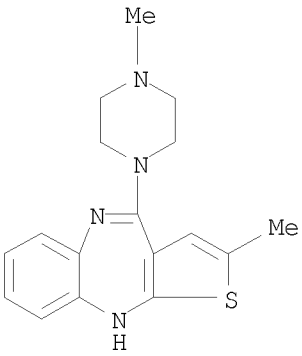
PRIORITY APPLN. INFO.: US 2002-160958 A 20020531
WO 2003-US17186 W 20030530
OTHER SOURCE(S): CASREACT 140:16753
GI



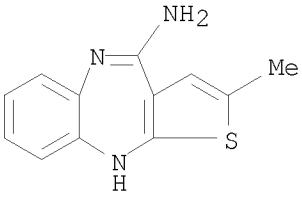
I

AB The title compound (I), an antipsychotic agent, was prepared from 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride and 1-methylpiperazine. A crystallization method yielded the polymorphic form I in 99.96% HPLC purity.
IT 132539-06-1P, Olanzapine

RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation of olanzapine form I)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of olanzapine form I)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)

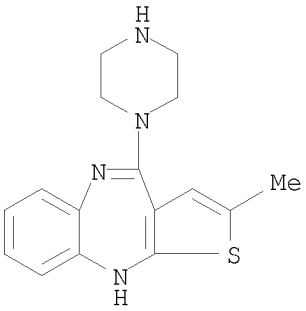


OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

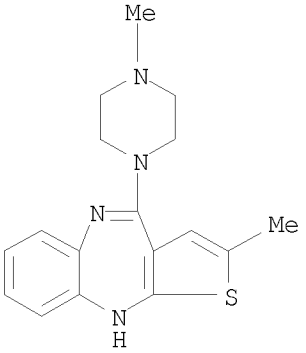
L31 ANSWER 17 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:967624 CAPLUS
DOCUMENT NUMBER: 140:399206
TITLE: An automated blood sampler for simultaneous sampling of systemic blood and brain microdialysates for drug absorption, distribution, metabolism, and elimination studies
AUTHOR(S): Gunaratna, P. Chandrani; Kissinger, Peter T.; Kissinger, Candice B.; Gitzen, James F.
CORPORATE SOURCE: Bioanalytical Systems, West Lafayette, IN, 47906-1382, USA
SOURCE: Journal of Pharmacological and Toxicological Methods (2004), 49(1), 57-64
CODEN: JPTMEZ; ISSN: 1056-8719
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A major problem in preclin. drug development where blood sampling from small animals is a routine practice is the time and labor involved in the serial sampling of small blood vols. from small animals such as rats for the duration of pharmacokinetic/pharmacodynamic (PK/PD) studies. The traditional method of manually drawing blood from the animal requires the animal to be anesthetized or restrained with some device, both of which cause stress to the animal. An automated blood sampler (ABS) was developed to simultaneously collect blood and brain microdialyzate samples at preprogrammed time points from awake and freely moving animals. The samples are delivered to fraction collectors and stored at 4° until use. The lost blood volume during collection is replaced with sterile saline to prevent fluid loss from the animal. In addition, the system is capable of collecting urine and feces for metabolism studies and monitoring the animal activity for behavioral studies. In the present study, blood samples were collected for 24 h after dosing rats orally with a 5 mg/kg dose of olanzapine (OLAN). Brain dialyzates were collected for the same duration from a microdialysis probe implanted in the striatum. The pharmacokinetic parameters, obtained after an oral dose, are in good agreement with reported values in literature. The pharmacodynamic information obtained from brain dialyzates data show that OLAN elevates the concentration of dopamine (DA) in the brain and remains in the brain even after it is cleared from the plasma. The ABS described here is a very useful tool in drug development to accelerate the pace of preclin. in vivo studies and to simultaneously provide pharmacodynamic and physiol. information.

IT 161696-76-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(automated blood sampler for simultaneous sampling of systemic blood and brain microdialyzates for pharmacokinetic/pharmacodynamic studies applied to olanzapine and its effects on levels of neurotransmiters)
RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



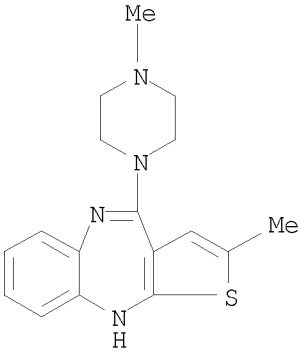
IT 132539-06-1, Olanzapine
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(automated blood sampler for simultaneous sampling of systemic blood and brain microdialyzates for pharmacokinetic/pharmacodynamic studies applied to olanzapine and its effects on levels of neurotransmiters)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-
(CA INDEX NAME)



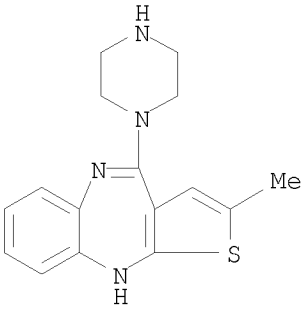
OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 18 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:851812 CAPLUS
DOCUMENT NUMBER: 140:246781
TITLE: Relationship between levels of insulin or triglycerides and serum concentrations of the atypical antipsychotics clozapine and olanzapine in patients on treatment with therapeutic doses
AUTHOR(S): Melkersson, K. I.; Dahl, M.-L.
CORPORATE SOURCE: Sollentuna Psychiatric Polyclinic, Department of Molecular Medicine, Karolinska Institute, Stockholm, Swed.
SOURCE: Psychopharmacology (Berlin, Germany) (2003), 170(2), 157-166
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rationale. Recent results suggest that treatment with the atypical antipsychotics clozapine and olanzapine is associated with increased insulin and lipid levels. Objective. The aim of the present study was to investigate potential relationships between insulin or other hormones related to glucose-insulin homeostasis or lipids and steady-state serum concns. of clozapine or olanzapine in patients on therapeutic doses. Methods. Thirty-four patients, diagnosed with schizophrenia or related psychoses according to the DSM-IV criteria and treated with clozapine (n=18) or olanzapine (n=16), were studied. Median treatment time with the antipsychotics was 5.3 yr (range 0.5-16.3 yr). Fasting blood samples for insulin, C-peptide, insulin-like growth factor I, insulin-like growth factor binding protein-1, leptin, glucose and lipids were analyzed and investigated in relation to the patients' drug serum concns. Results. Hyperinsulinemia was found in 30-60% of the patients, hyperglycemia in 10-30%, hyperlipidemia in 40-60% and hyperleptinemia in 10-20%. Moreover, levels of insulin, C-peptide and triglycerides correlated pos. to the clozapine serum concentration and to the ratio of olanzapine to N-desmethylolanzapine concns. In contrast, levels of C-peptide, leptin and blood glucose were inversely correlated to the serum concentration of the metabolite N-desmethylolanzapine. Conclusions. Metabolic abnormalities (i.e. hyperinsulinemia, hyperlipidemia and hyperleptinemia) and insulin resistance were associated with both clozapine and olanzapine treatments. Levels of insulin and triglycerides increased by increasing clozapine serum concentration and by increasing ratio of olanzapine to N-desmethylolanzapine; the last due to the metabolite N-desmethylolanzapine probably having an inverse effect to the main compound olanzapine. Thus, the metabolic abnormalities induced by these two drugs are clozapine-concentration dependent in clozapine-treated patients, and ratio of olanzapine to N-desmethylolanzapine-concentration dependent in olanzapine-treated patients.
IT 132539-06-1, Olanzapine
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(relationship between levels of insulin or triglycerides and serum concns. of the atypical antipsychotics clozapine and olanzapine in patients on treatment with therapeutic doses)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-

(CA INDEX NAME)



IT 161696-76-0, N-Demethylolanzapine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(relationship between levels of insulin or triglycerides and serum concns. of the atypical antipsychotics clozapine and olanzapine in patients on treatment with therapeutic doses)
RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



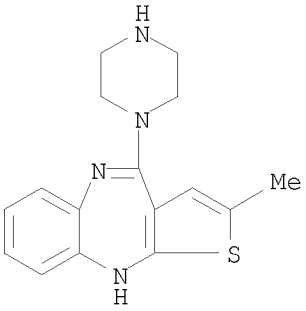
OS.CITING REF COUNT: 33 THERE ARE 33 CAPLUS RECORDS THAT CITE THIS RECORD (33 CITINGS)
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 19 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:747138 CAPLUS
DOCUMENT NUMBER: 139:392238
TITLE: Toxicological Screening with Formula-Based Metabolite Identification by Liquid Chromatography/Time-of-Flight Mass Spectrometry
AUTHOR(S): Pelander, Anna; Ojanperae, Ilkka; Laks, Suvi; Rasanen, Ilpo; Vuori, Erkki
CORPORATE SOURCE: Department of Forensic Medicine, University of Helsinki, FIN-00014, Finland
SOURCE: Analytical Chemistry (2003), 75(21), 5710-5718
CODEN: ANCHAM; ISSN: 0003-2700
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

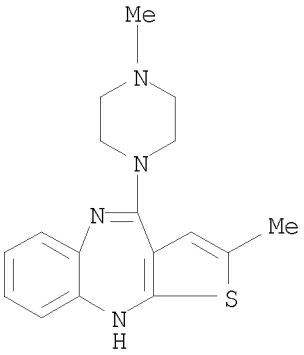
AB An anal. procedure was evaluated for the comprehensive toxicol. screening of drugs, metabolites, and pesticides in 1-mL urine samples by TurboIon spray liquid chromatog./time-of-flight mass spectrometry (LC/TOFMS) in the pos. ionization mode and continuous mass measurement. The substance database consisted of exact monoisotopic masses for 637 compds., of which an LC retention time was available for 392. A macroprogram was refined for extracting the data into a legible report, utilizing metabolic patterns and preset identification criteria. These criteria included ±30 ppm mass tolerance, a ±0.2-min window for absolute retention time, if available, and a min. area count of 500. The limit of detection, determined for 90 compds., was <0.1 mg/L for 73% of the compds. studied and >1.0 mg/L for 6% of the compds. For method comparisons, 50 successive autopsy urine samples were analyzed by this method, and the results confirmed by gas chromatog./mass spectrometry (GC/MS). Findings for parent drugs were consistent with both methods; in addition, LC/TOFMS regularly revealed apparently correct findings for metabolites not shown by GC/MS. Mean and median mass accuracy by LC/TOFMS was 7.6 and 5.4 ppm, resp. The procedure proved well-suited for tentative identification without reference substances. The few false positives emphasized the fact that all three parameters, exact mass, retention time, and metabolite pattern, are required for unequivocal identification.

IT 161696-76-0
RL: ANT (Analyte); ANST (Analytical study)
(toxicol. screening of drugs and metabolites in urine samples with formula-based metabolite identification by liquid chromatog./time-of-flight mass spectrometry)

RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



IT 132539-06-1, Olanzapine
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(toxicol. screening of drugs and metabolites in urine samples with formula-based metabolite identification by liquid chromatog./time-of-flight mass spectrometry)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



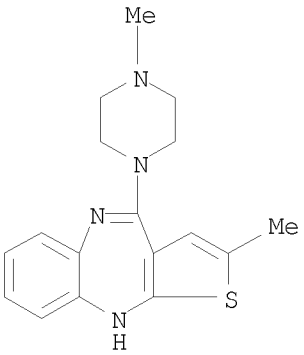
OS.CITING REF COUNT:	50	THERE ARE 50 CAPLUS RECORDS THAT CITE THIS RECORD (50 CITINGS)
REFERENCE COUNT:	20	THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 20 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:325864 CAPLUS
DOCUMENT NUMBER: 139:303082
TITLE: Evaluation of electrospray ionisation liquid chromatography-tandem mass spectrometry for rational determination of a number of neuroleptics and their major metabolites in human body fluids and tissues
AUTHOR(S): Josefsson, M.; Kronstrand, R.; Andersson, J.; Roman, M.
CORPORATE SOURCE: Department of Forensic Chemistry, National Board of Forensic Medicine, University Hospital, Linkoping, SE-581 85, Swed.
SOURCE: Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2003), 789(1), 151-167
CODEN: JCBAAI; ISSN: 1570-0232
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

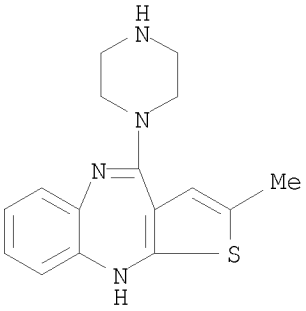
AB A study of liquid chromatog.-triple quadrupole mass spectrometry (LC-MS-MS) with pos. electrospray ionization (ESI) for the determination of selected drugs in human tissues and body fluids such as blood, urine and hair is described. The possibility to screen for and quantify the 19 most commonly prescribed neuroleptics on the Swedish market and determine the presence of their major metabolites within a single LC-MS-MS anal. was evaluated on a PE Sciex API2000 instrument. Chromatog. conditions were optimized and the best separation, with individual retention times for most of the analytes, was obtained on a Zorbax SB-CN column within a 9-min gradient run. The MS-MS fragmentation conditions were optimized for each compound in order to obtain both specific fragments and high signal intensity. Since neuroleptics are a heterogeneous group of compds., a markedly difference in collision energy needed to achieve fragments of the selected parent ions was seen and the number of fragments achieved varied as well. For sensitive quantification the transition of the most intense fragment of the protonated mol. ion (M+1)+ was selected for multiple reaction monitoring anal. More than 70 transitions were finally included in the assay. Detection levels down to the lower ng/mL level were achieved for all analytes, but between analytes more than a 10-fold difference in signal response was seen. By evaluation of extracted ion chromatograms from the anal. of authentic human blood, urine and hair sample the proposed concept for rational drug anal. was found to be both selective and sensitive for the neuroleptics included. A great number of metabolites could be determined in blood, urine and hair as well. A full method validation was not performed since the objective was to evaluate the method design rather than to validate a final method set-up.

IT 132539-06-1, Olanzapine 161696-76-0
RL: ANT (Analyte); ANST (Analytical study)
(evaluation of electrospray ionization LC-tandem MS for rational determination of neuroleptics and their major metabolites in human body fluids and tissues)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)

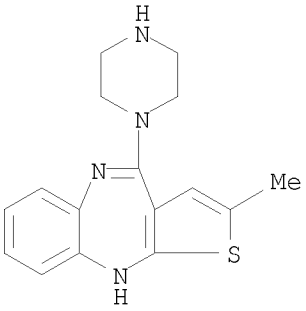


OS.CITING REF COUNT:	23	THERE ARE 23 CAPLUS RECORDS THAT CITE THIS RECORD (24 CITINGS)
REFERENCE COUNT:	28	THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

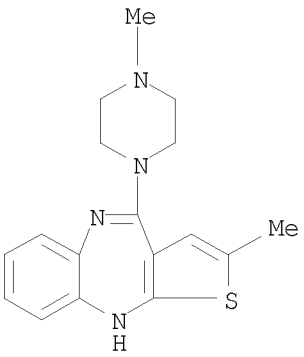
L31 ANSWER 21 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:739041 CAPLUS
DOCUMENT NUMBER: 139:330
TITLE: Fluvoxamine Augmentation of Olanzapine in Chronic Schizophrenia: Pharmacokinetic Interactions and Clinical Effects
AUTHOR(S): Hiemke, Christoph; Peled, Avi; Jabarin, Mahmoud; Hadjez, Jack; Weigmann, Harald; Haertter, Sebastian; Modai, Ilan; Ritsner, Michael; Silver, Henry
CORPORATE SOURCE: Dep. of Psychiatry, Univ. of Mainz, Mainz, Germany
SOURCE: Journal of Clinical Psychopharmacology (2002), 22(5), 502-506
CODEN: JCPYDR; ISSN: 0271-0749
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Olanzapine is a substrate of the cytochrome P 450 enzyme (CYP) 1A2. In this study, pharmacokinetic interactions and clin. effects of adding the CYP1A2 inhibitor fluvoxamine to steady-state olanzapine was examined in patients suffering from schizophrenia. Eight patients had been treated for at least 3 mo with 10 to 20 mg/day olanzapine. Fluvoxamine (100 mg/day) was added (week 0) to the olanzapine treatment and continued for 8 wk. Concns. of olanzapine and its metabolite N-desmethylolanzapine and of fluvoxamine were analyzed at weeks 0, 1, 4, and 8. Addition of fluvoxamine resulted in a 12% to 112% ($p < 0.01$) increase of olanzapine from 31 ± SD 15 ng/mL (week 0) to 56 ± 31 ng/mL (week 8) in all patients. N-desmethylolanzapine concns. were not significantly changed ($p > 0.05$). Fluvoxamine concns. were 48 ± 26 ng/mL on week 1 and 83 ± 47 ng/mL on week 8. It is concluded that fluvoxamine affects olanzapine degradation and thus increases olanzapine concns. Although the combination was well tolerated in this sample and the neg. symptom response appeared to be favorable in at least five patients, the combination therapy of olanzapine and fluvoxamine should be used cautiously and should be controlled by therapeutic drug monitoring to avoid olanzapine-induced side effects or intoxications.

IT 161696-76-0, N-Demethylolanzapine
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)
(olanzapine metabolite; pharmacokinetic interactions and clin. effects in fluvoxamine augmentation of olanzapine in chronic schizophrenia)
RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)

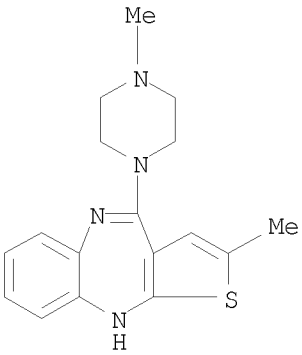


IT 132539-06-1, Olanzapine
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetic interactions and clin. effects in fluvoxamine augmentation of olanzapine in chronic schizophrenia)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

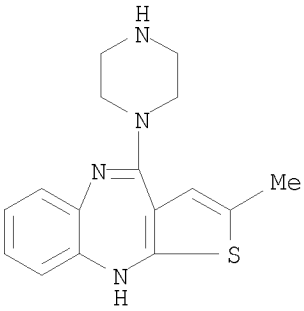


OS.CITING REF COUNT:	26	THERE ARE 26 CAPLUS RECORDS THAT CITE THIS RECORD (26 CITINGS)
REFERENCE COUNT:	40	THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 22 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:642690 CAPLUS
DOCUMENT NUMBER: 137:272772
TITLE: Therapeutic drug monitoring data on olanzapine and its N-demethyl metabolite in the naturalistic clinical setting
AUTHOR(S): Skogh, Elisabeth; Reis, Margareta; Dahl, Marja-Liisa; Lundmark, Joens; Bengtsson, Finn
CORPORATE SOURCE: Division of Psychiatry, Department of Neuroscience and Locomotion, Faculty of Health Sciences, Linkoeping University, Linkoeping, Swed.
SOURCE: Therapeutic Drug Monitoring (2002), 24(4), 518-526
CODEN: TDMODV; ISSN: 0163-4356
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Olanzapine (Zyprexa) was approved for general prescription in Sweden in Nov. 1996, and an HPLC-based therapeutic drug monitoring (TDM) routine for serum olanzapine (OLA) and its major metabolite, N-demethylolanzapine (DMO) was established in Feb. 1997. During 1997 to 1999, a total of 753 TDM requests for a total of 545 Swedish patients was analyzed. Addnl. patient information on certain clin. variables was collected on specifically designed TDM request forms. After the exclusion process, samples from 194 patients were found to be eligible for further scrutiny. The concentration-to-dose (C/D) ratio for OLA varied 25-fold and that of DMO 22-fold. Women had a higher ($P < 0.01$) median C/D ratio for OLA than men (median, 7.2 nmol/L/mg vs. 5.2 nmol/L/mg). Nonsmokers had a higher ($P < 0.001$) C/D ratio for OLA than smokers (median, 9.2 nmol/L/mg vs 4.0 nmol/L/mg). Smokers got higher prescribed ($P < 0.05$) doses of OLA than nonsmokers did. In the group with reported side effects, the median serum OLA concentration was 22% higher ($P < 0.05$) than in the group without side effects. Patients co-medicated with carbamazepine had a 71 % lower median C/D ratio for OLA than patients on OLA monotherapy. The present TDM-based follow-up suggests that the influence of gender, smoking habits, and certain drug interactions may need to be considered for optimal dosage of OLA. TDM may be used for this purpose more readily in the future.
IT 132539-06-1, Zyprexa
RL: ADV (Adverse effect, including toxicity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic drug monitoring data on olanzapine and its N-demethyl metabolite in humans)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 161696-76-0, N-Demethylolanzapine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(therapeutic drug monitoring data on olanzapine and its N-demethyl metabolite in humans)
RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



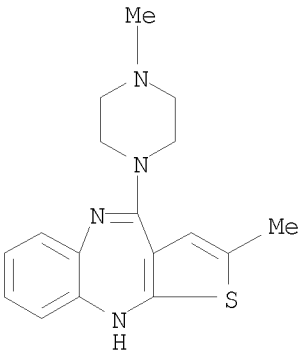
OS.CITING REF COUNT: 30 THERE ARE 30 CAPLUS RECORDS THAT CITE THIS RECORD (31 CITINGS)
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 23 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:336083 CAPLUS
DOCUMENT NUMBER: 137:304266
TITLE: Three-dimensional quantitative structure-activity relationship for inhibition of human ether-a-go-go-related gene potassium channel
AUTHOR(S): Ekins, Sean; Crumb, William J.; Sarazan, R. Dustan; Wikel, James H.; Wrighton, Steven A.
CORPORATE SOURCE: Lilly Research Laboratories, Lilly Corporate Center, Eli Lilly and Co., Indianapolis, IN, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 301(2), 427-434
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

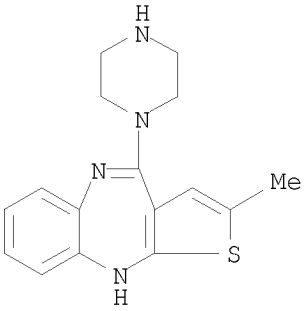
AB The protein product of the human ether-a-go-go gene (hERG) is a potassium channel that when inhibited by some drugs may lead to cardiac arrhythmia. Previously, a three-dimensional quant. structure-activity relationship (3D-QSAR) pharmacophore model was constructed using Catalyst with in vitro inhibition data for antipsychotic agents. The rationale of the current study was to use a combination of in vitro and in silico technologies to further test the pharmacophore model and qual. predict whether mols. are likely to inhibit this potassium channel. These predictions were assessed with the exptl. data using the Spearman's rho rank correlation. The antipsychotic-based hERG inhibitor model produced a statistically significant Spearman's rho of 0.71 for 11 mols. In addition, 15 mols. from the literature were used as a further test set and were also well ranked by the same model with a statistically significant Spearman's rho value of 0.76. A Catalyst General hERG pharmacophore model was generated with these literature mols., which contained four hydrophobic features and one pos. ionizable feature. Linear regression of log-transformed observed vs. predicted IC50 values for this training set resulted in an r2 value of 0.90. The model based on literature data was evaluated with the in vitro data generated for the original 22 mols. (including the antipsychotics) and illustrated a significant Spearman's rho of 0.77. Thus, the Catalyst 3D-QSAR approach provides useful qual. predictions for test set mols. The model based on literature data therefore provides a potentially valuable tool for discovery chemical as future mols. may be synthesized that are less likely to inhibit hERG based on information provided by a pharmacophore for the inhibition of this potassium channel.

IT 132539-06-1, Olanzapine 161696-76-0
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(three-dimensional quant. structure-activity relationship for inhibition of human ether-a-go-go-related gene potassium channel)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



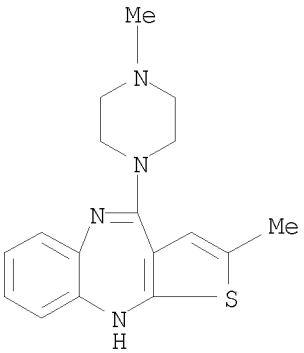
OS.CITING REF COUNT:	137	THERE ARE 137 CAPLUS RECORDS THAT CITE THIS RECORD (141 CITINGS)
REFERENCE COUNT:	30	THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 24 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:688684 CAPLUS
DOCUMENT NUMBER: 136:106
TITLE: Determination of olanzapine and desmethylolanzapine in the plasma of schizophrenic patients by means of an improved HPLC method with amperometric detection
AUTHOR(S): Raggi, M. A.; Mandrioli, R.; Sabbioni, C.; Ghedini, N.; Fanali, S.; Volterra, V.
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Bologna, Bologna, 40126, Italy
SOURCE: Chromatographia (2001), 54(3/4), 203-207
CODEN: CHRGB7; ISSN: 0009-5893
PUBLISHER: Friedrich Vieweg & Sohn Verlagsgesellschaft mbH
DOCUMENT TYPE: Journal
LANGUAGE: English

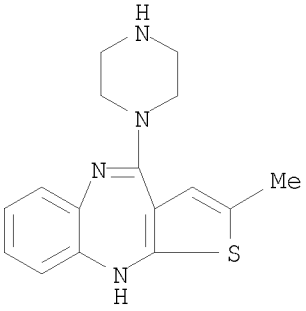
AB An improved HPLC method with electrochem. detection was developed for the determination of olanzapine and its main metabolite, desmethylolanzapine, in human plasma. Chromatog. separation and anal. were performed on a C8 reversed-phase column with a mixture of MeOH, MeCN, and pH 3.7 phosphate buffer as mobile phase; 2-methylolanzapine was used as internal standard Careful pretreatment of the plasma samples was implemented by solid phase extraction (SPE). Response was linearly dependent on concentration and precision was satisfactory over the concentration range 0.5-75.0 ng mL-1 for both analytes. The limit of detection was 0.2 ng mL-1 for both analytes. Application to plasma samples of patients treated with Zyprexa tablets gave good results. Because of its sensitivity and selectivity, and the need for small plasma samples, this method seems to be a useful tool for clin. monitoring.

IT 132539-06-1, Olanzapine 161696-76-0
RL: ANT (Analyte); ANST (Analytical study)
(determination of olanzapine and desmethylolanzapine in the plasma of schizophrenic patients by means of an improved HPLC method with amperometric detection)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

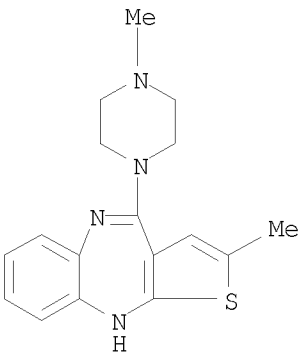


RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)

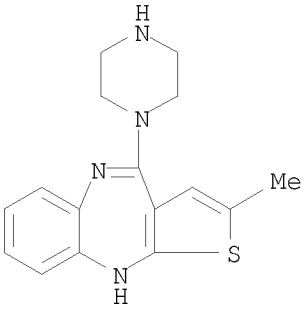


OS.CITING REF COUNT:	10	THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT:	16	THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 25 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:467184 CAPLUS
DOCUMENT NUMBER: 135:298072
TITLE: Simultaneous determination of olanzapine, clozapine and demethylated metabolites in serum by on-line column-switching high-performance liquid chromatography
AUTHOR(S): Weigmann, H.; Hartter, S.; Maehrlein, S.; Kiefer, W.; Kramer, G.; Dannhardt, G.; Hiemke, C.
CORPORATE SOURCE: Department of Psychiatry, University of Mainz, Mainz, D-55131, Germany
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 759(1), 63-71
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An automated method for simultaneous routine quantification of the antipsychotic drugs clozapine, olanzapine and their demethylated metabolites is described. The method included adsorption on a cyanopropyl (CPS) coated clean-up column (10 μm; 10+2.0 mm I.D.), washing off interfering serum constituents to waste, and separation on C18 ODS Hypersil reversed phase material (5 μm; 250+4.6 mm I.D.) using MeCN-H2O-tetramethylethylenediamine (37:62.6:0.4, volume/volume/v) adjusted to pH 6.5 with concentrated HOAc. UV-detection was performed at 254 nm. The limit of quantification was 10-20 ng/mL. Relative day to day standard variations ranged between 4.5 and 13.5%. The method is suitable for routine monitoring of olanzapine and clozapine including their demethylated metabolites.
IT 132539-06-1, Olanzapine 161696-76-0
RL: ANT (Analyte); ANST (Analytical study)
(simultaneous determination of olanzapine, clozapine and demethylated metabolites in serum by online column-switching high-performance liquid chromatog.)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



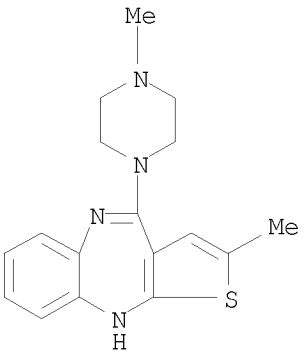
OS.CITING REF COUNT:	32	THERE ARE 32 CAPLUS RECORDS THAT CITE THIS RECORD (32 CITINGS)
REFERENCE COUNT:	55	THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 26 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:112809 CAPLUS
DOCUMENT NUMBER: 135:40320
TITLE: Separation of olanzapine, carbamazepine and their main metabolites by capillary electrophoresis with pseudo-stationary phases
AUTHOR(S): Izzo, G.; Raggi, M.-A.; Maichel, B.; Kenndler, E.
CORPORATE SOURCE: Institute for Analytical Chemistry, University of Vienna, Vienna, A-1090, Austria
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 752(1), 47-53
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Conditions were worked out for the separation of carbamazepine, olanzapine, and their main metabolites carbamazepine 10,11-epoxide, 10-hydroxycarbamazepine, and desmethylolanzapine. The separation was based on electrokinetically driven methods in the capillary format. The main difficulty in separating these compds. is related to their different chemical classes. Whereas the carbamazepine members are amides, and are elec. neutral, the olanzapine members have aliphatic amino groups and are thus cationic under most exptl. conditions. Different additives were applied as pseudo-stationary phases to implement selectivity. Poly(diallyldimethylammonium), PDADMA, is a polycationic replaceable and soluble polymer, that interacts mainly according to the polarizability of the analyte mols. The MEKC principle was applied with the common SDS as micelle former. In both systems, only partial resolution of the analytes was obtained. The most favorable system consisted of a charged, oligomeric additive: full separation of all analytes within 4 min was achieved with heptakis-6-sulfato-β-cyclodextrin (7 mM) in 30 mM borate buffer, pH 8.5.

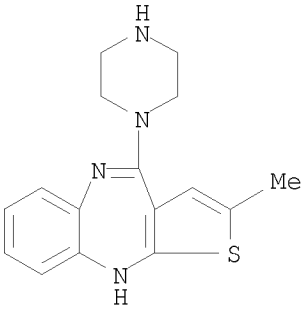
IT 132539-06-1P, Olanzapine 161696-76-0P
RL: ANT (Analyte); PUR (Purification or recovery); ANST (Analytical study); PREP (Preparation)
(separation of olanzapine, carbamazepine and their main metabolites by capillary electrophoresis with pseudo-stationary phases)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



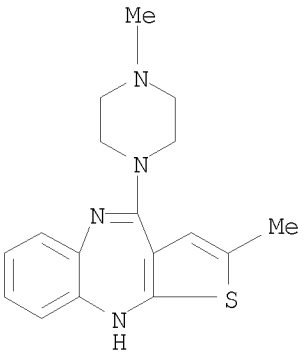
RN 161696-76-0 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)

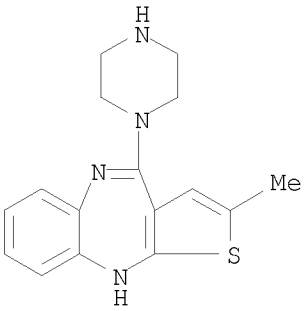


OS.CITING REF COUNT:	16	THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT:	27	THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 27 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:858332 CAPLUS
DOCUMENT NUMBER: 135:55877
TITLE: Elevated levels of insulin, leptin, and blood lipids in olanzapine-treated patients with schizophrenia or related psychoses
AUTHOR(S): Melkersson, Kristina I.; Hulting, Anna-Lena; Brismar, Kerstin E.
CORPORATE SOURCE: Dep. of Psychiatry, St. Gorans Hosp., Stockholm, Swed.
SOURCE: Journal of Clinical Psychiatry (2000), 61(10), 742-749
CODEN: JCLPDE; ISSN: 0160-6689
PUBLISHER: Physicians Postgraduate Press, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: The aim of this study was to investigate the influence of the antipsychotic agent olanzapine on glucose-insulin homeostasis to explain possible mechanisms behind olanzapine-associated weight gain. Method: Fourteen patients on treatment with olanzapine (all meeting DSM-IV criteria for schizophrenia or related psychoses) were studied. Fasting blood samples for glucose, insulin, the growth hormone (GH)-dependent insulin-like growth factor I, and the insulin-dependent insulin-like growth factor binding protein-1 (IGFBP-1) were analyzed, as well as GH, leptin, and blood lipid levels and the serum concns. of olanzapine and its metabolite N-desmethylolanzapine. In addition, body mass index (BMI) was calculated Moreover, weight change during olanzapine treatment was determined Results: Twelve of the 14 patients reported weight gain between 1 and 10 kg during a median olanzapine treatment time of 5 mo, whereas data were not available for the other 2 patients. Eight patients (57%) had BMI above the normal limit. Eleven patients were normoglycermic, and 3 showed increased blood glucose values. Most patients (10/14; 71%) had elevated insulin levels (i.e., above the normal limit). Accordingly, the median value of IGFBP-1 was significantly lower for the patients in comparison with healthy subjects. Moreover, 8 (57%) of 14 patients had hyperleptinemia, 62% (8/13) had hypertriglyceridemia, and 85% (11/13) hypercholesterolemia. Weight change correlated pos. to blood glucose levels and inversely to the serum concentration level of N-desmethylolanzapine. Addnl., the levels of blood glucose, triglycerides, and cholesterol correlated inversely to the serum concentration of N-desmethylolanzapine. Conclusion: Olanzapine treatment was associated with weight gain and elevated levels of insulin, leptin, and blood lipids as well as insulin resistance, with 3 patients diagnosed to have diabetes mellitus. Both increased insulin secretion and hyperleptinemia may be mechanisms behind olanzapine-induced weight gain. Moreover, it is suggested that the metabolite N-desmethylolanzapine, but not olanzapine, has a normalizing effect on the metabolic abnormalities.
IT 132539-06-1, Olanzapine
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(insulin, leptin, and blood lipids elevated levels in olanzapine-treated humans with schizophrenia or related psychoses)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 161696-76-0
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(insulin, leptin, and blood lipids elevated levels in olanzapine-treated humans with schizophrenia or related psychoses)
RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 106 THERE ARE 106 CAPLUS RECORDS THAT CITE THIS RECORD (106 CITINGS)
REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 28 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:227510 CAPLUS
DOCUMENT NUMBER: 132:256034
TITLE: 2-Methylthienobenzodiazepine formulation
INVENTOR(S): Bunnell, Charles Arthur; Ferguson, Thomas Harry; Hendriksen, Barry Arnold; Sanchez-Felix, Manuel Vicente; Tupper, David Edward
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018408	A1	20000406	WO 1999-US6417	19990324
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6169084	B1	20010102	US 1998-163769	19980930
CA 2344873	A1	20000406	CA 1999-2344873	19990324
AU 9933627	A	20000417	AU 1999-33627	19990324
AU 759751	B2	20030501		
BR 9914156	A	20010626	BR 1999-14156	19990324
EP 1119359	A1	20010801	EP 1999-915009	19990324
EP 1119359	B1	20040526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200100885	T2	20010821	TR 2001-885	19990324
HU 2001003636	A2	20020128	HU 2001-3636	19990324
HU 2001003636	A3	20030528		
JP 2002525330	T	20020813	JP 2000-571926	19990324
NZ 510208	A	20030429	NZ 1999-510208	19990324
CN 1146422	C	20040421	CN 1999-811535	19990324
AT 267602	T	20040615	AT 1999-915009	19990324
EP 1468689	A1	20041020	EP 2004-5832	19990324
EP 1468689	B1	20070418		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
ES 2221376	T3	20041216	ES 1999-915009	19990324
IL 141766	A	20061231	IL 1999-141766	19990324
AT 359793	T	20070515	AT 2004-5832	19990324
SK 285944	B6	20071102	SK 2001-416	19990324
ES 2285294	T3	20071116	ES 2004-5832	19990324
PL 196821	B1	20080229	PL 1999-346981	19990324
TW 577890	B	20040301	TW 1999-88105028	19990402
ZA 2001002231	A	20020318	ZA 2001-2231	20010316
IN 2001CN00338	A	20050311	IN 2001-CN338	20010326
NO 2001001583	A	20010328	NO 2001-1583	20010328
MX 2001003288	A	20011011	MX 2001-3288	20010329

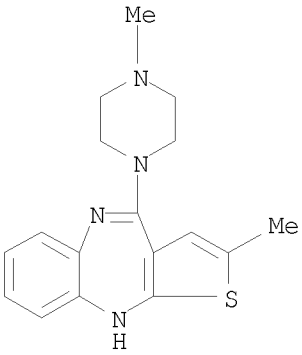
HR 2001000238	A1	20020430	HR 2001-238		20010329
HR 2001000238	B1	20060531			
HK 1041199	A1	20050318	HK 2002-100774		20020131
PRIORITY APPLN. INFO.:			US 1998-163768	A	19980930
			US 1998-163769	A	19980930
			US 1997-60493P	P	19970930
			EP 1999-915009	A3	19990324
			WO 1999-US6417	W	19990324

AB The invention provides a pharmaceutically acceptable oleaginous or cholesterol microsphere formulation of olanzapine or olanzapine pamoate or solvates. Thus, olanzapine was prepared and mixed with cholesterol in methylene chloride. An aqueous solution of PVA was added to the above solution and the mixture was passed through 100- and 230-mesh sieves, and the particles thus obtained were allowed to dry.

IT 132539-06-1P, Olanzapine
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(methylthienobenzodiazepine formulations)

RN 132539-06-1 CAPLUS

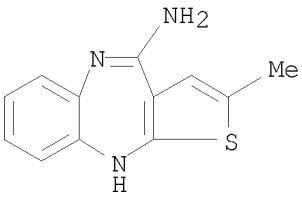
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(methylthienobenzodiazepine formulations)

RN 138564-60-0 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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OS.CITING REF COUNT:	4	THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT:	1	THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

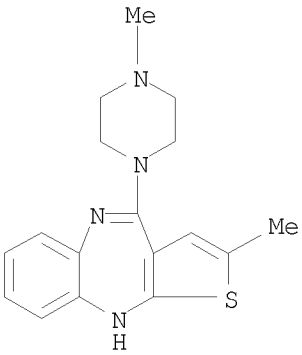
L31 ANSWER 29 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:752863 CAPLUS
DOCUMENT NUMBER: 131:346550
TITLE: Atypical antipsychotic agent-serotonin reuptake inhibitor combinations for therapy of refractory depression
INVENTOR(S): Tollefson, Gary Dennis
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 958824	A2	19991124	EP 1999-303969	19990521
EP 958824	A3	19991201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200003443	T2	20010321	TR 2000-3443	19990521
CN 1154496	C	20040623	CN 1999-809071	19990521
TW 226829	B	20050121	TW 1999-88108382	19990521
ZA 2000006815	A	20020114	ZA 2000-6815	20001121

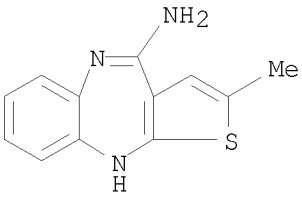
PRIORITY APPLN. INFO.: US 1998-86444P P 19980522

AB Methods and compns. are provided for the treatment of depressive states refractory to treatment with traditional antidepressive therapies alone. These methods and compns. employ a compound having activity as an atypical antipsychotic (e.g. olanzapine) and a serotonin reuptake inhibitor (e.g. fluoxetine). This invention also provides methods of providing rapid onset treatments of major depression which employing a compound having activity as an atypical antipsychotic and a serotonin reuptake inhibitor.

IT 132539-06-1P, Olanzapine
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(atypical antipsychotic agent-serotonin reuptake inhibitor combinations for therapy of refractory depression)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; atypical antipsychotic agent-serotonin reuptake inhibitor combinations for therapy of refractory depression)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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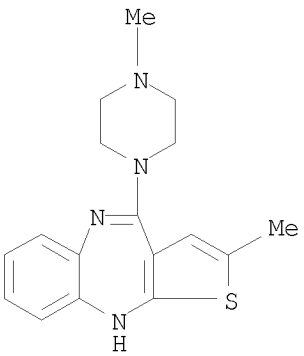
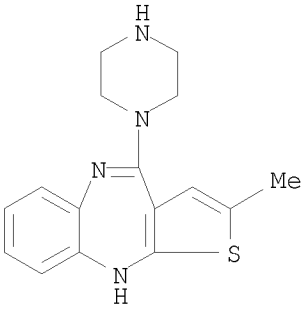
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

L31 ANSWER 30 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:607839 CAPLUS
DOCUMENT NUMBER: 132:64
TITLE: Monitoring of olanzapine in serum by liquid chromatography-atmospheric pressure chemical ionization mass spectrometry
AUTHOR(S): Bogusz, M. J.; Kruger, K. D.; Maier, R. D.; Erkwoh, R.; Tuchtenhagen, F.
CORPORATE SOURCE: Klinikum RWTH, Institute of Forensic Medicine, Aachen University of Technology, Aachen, 52057, Germany
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (1999), 732(2), 257-269
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A selective HPLC-MS assay of olanzapine in human blood serum or urine is described. The drug and internal standard (Et derivative of olanzapine) were isolated from the samples by solid-phase extraction on C18 cartridges. The separation was performed on ODS column in acetonitrile-50 mM ammonium formate buffer, pH 3.0 (25:75). After anal. of mass spectra taken in full scan mode, a selected-ion monitoring detection (SIM) was applied with the following ions: m/z 313 and 256 for olanzapine and m/z 327 and 270 for the internal standard for quantitation. The limit of quantitation was 1 μg/L and the absolute recovery was >80% at concns. 10-100 μg/L. The method was linear in the range of 1-1000 μg/L and was applied for therapeutic monitoring of olanzapine in the blood serum of psychiatric patients treated with Zyprexa and in one case of olanzapine overdose. Olanzapine in frozen serum samples and in frozen exts. was stable for at least 4 wk. Urine exts. from patients receiving olanzapine contained postulated olanzapine metabolites (glucuronide and N-desmethylolanzapine).
IT 132539-06-1, Olanzapine 161696-76-0
RL: ANT (Analyte); ANST (Analytical study)
(olanzapine determination in blood serum by HPLC-atmospheric pressure chemical ionization
MS)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA

INDEX NAME)



OS.CITING REF COUNT:	43	THERE ARE 43 CAPLUS RECORDS THAT CITE THIS RECORD (44 CITINGS)
REFERENCE COUNT:	29	THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

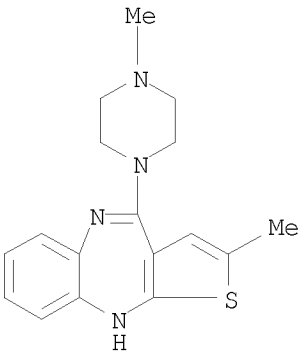
L31 ANSWER 31 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:425470 CAPLUS
DOCUMENT NUMBER: 131:78439
TITLE: Oral formulations containing olanzapine
INVENTOR(S): Cochran, George Randall; Morris, Tommy Clifford
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S., 7 pp., Cont.-in-part of U.S. Ser. No. 410,465, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5919485	A	19990706	US 1996-716922	19960920
EG 24077	A	20080511	EG 1996-251	19960321
CA 2216372	A1	19961003	CA 1996-2216372	19960322
CA 2216372	C	20071120		
WO 9629995	A1	19961003	WO 1996-US3918	19960322
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9654280	A	19961016	AU 1996-54280	19960322
AU 696601	B2	19980917		
ZA 9602338	A	19970922	ZA 1996-2338	19960322
GB 2313783	A	19971210	GB 1997-19817	19960322
GB 2313783	B	19981118		
DE 19681287	T0	19980319	DE 1996-19681287	19960322
CN 1179102	A	19980415	CN 1996-192778	19960322
CN 1178662	C	20041208		
BR 9607791	A	19980707	BR 1996-7791	19960322
HU 9800410	A2	19980728	HU 1998-410	19960322
HU 9800410	A3	20000128		
HU 225269	B1	20060828		
AT 9609022	A	19990215	AT 1996-9022	19960322
AT 405606	B	19991025		
JP 11502848	T	19990309	JP 1996-529533	19960322
TW 426526	B	20010321	TW 1996-85103453	19960322
CH 691217	A5	20010531	CH 1997-2246	19960322
AT 206924	T	20011115	AT 1996-301997	19960322
EE 3551	B1	20011217	EE 1997-328	19960322
ES 2164837	T3	20020301	ES 1996-301997	19960322
IL 117611	A	20020523	IL 1996-117611	19960322
RO 118370	B1	20030530	RO 1997-1776	19960322
SK 283745	B6	20031202	SK 1997-1282	19960322
AT 284695	T	20050115	AT 2000-204708	19960322
PL 188316	B1	20050131	PL 1996-322579	19960322
ES 2232379	T3	20050601	ES 2000-204708	19960322
CZ 296007	B6	20051214	CZ 1997-3001	19960322
IN 1996CA00517	A	20060113	IN 1996-CA517	19960322
SE 9703206	A	19970905	SE 1997-3206	19970905
LT 4350	B	19980525	LT 1997-149	19970916

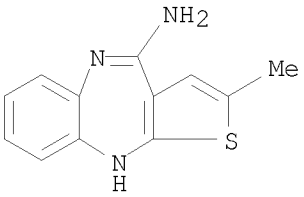
FI 9703749	A	19970922	FI 1997-3749		19970922
NO 9704363	A	19971117	NO 1997-4363		19970922
NO 320388	B1	20051128			
DK 9701090	A	19971112	DK 1997-1090		19970923
DK 173323	B1	20000724			
LV 11983	B	19980720	LV 1997-199		19971014
US 6190698	B1	20010220	US 1998-144188		19980831
IN 1999CA00416	A	20050311	IN 1999-CA416		19990504
US 20010018071	A1	20010830	US 2001-766218		20010119
US 6780433	B2	20040824			
US 20050085462	A1	20050421	US 2004-887017		20040708
US 7229643	B2	20070612			
IN 2007KO00577	A	20071026	IN 2007-KO577		20070413
PRIORITY APPLN. INFO.:			US 1995-410465	B2	19950324
			IN 1996-CA517	A3	19960322
			WO 1996-US3918	W	19960322
			US 1996-716922	A3	19960920
			US 1998-144188	A3	19980831
			US 2001-766218	A1	20010119

AB The invention provides a pharmaceutically acceptable solid oral formulation of olanzapine and a process for making such formulation. A preferred formulation of the invention is a solid oral formulation comprising 1-20 mg olanzapine, wherein such solid oral formulation is coated with hydroxypropyl Me cellulose. The coating provides a phys. stability and effectively prevents the undesired discoloration phenomenon in the formulation.

IT 132539-06-1P, Olanzapine
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Form II polymorph; polymer-coated oral formulations containing olanzapine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of olanzapine and polymer-coated tablet formulations for)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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OS.CITING REF COUNT:	6	THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT:	4	THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 32 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:233762 CAPLUS
DOCUMENT NUMBER: 130:257362
TITLE: Methylthienobenzodiazepine derivative antipsychotic drug formulation.
INVENTOR(S): Allen, Douglas James; Dekemper, Kurt Douglas; Ferguson, Thomas Harry; Garvin, Stuart James; Murray, Linda Cameron; Brooks, Norman Dale; Bunnell, Charles Arthur; Hendriksen, Barry Arnold; Mascarenhas, Snehlata Singh; Shinkle, Sharon Louise; Sanchez-Felix, Manuel Vicente; Tupper, David Edward
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9916313	A1	19990408	WO 1998-US20426	19980930
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2304568	A1	19990408	CA 1998-2304568	19980930
CA 2304568	C	20080812		
AU 9895914	A	19990423	AU 1998-95914	19980930
AU 752552	B2	20020919		
EP 1018880	A1	20000719	EP 1998-949632	19980930
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9813228	A	20000829	BR 1998-13228	19980930
HU 2000004534	A2	20010528	HU 2000-4534	19980930
TR 200000812	T2	20010723	TR 2000-812	19980930
JP 2001517685	T	20011009	JP 2000-513467	19980930
NZ 503641	A	20020927	NZ 1998-503641	19980930
CN 1239158	C	20060201	CN 1998-809565	19980930
IL 135295	A	20061031	IL 1998-135295	19980930
CZ 300725	B6	20090729	CZ 2000-1162	19980930
MX 2000003040	A	20001110	MX 2000-3040	20000328
NO 2000001631	A	20000530	NO 2000-1631	20000329
HR 2000000181	A1	20001231	HR 2000-181	20000331
HR 2000000181	B1	20060731		
US 20030027816	A1	20030206	US 2002-136887	20020501
US 6617321	B2	20030909		
US 20040097489	A1	20040520	US 2003-613619	20030703
US 7303764	B2	20071204		

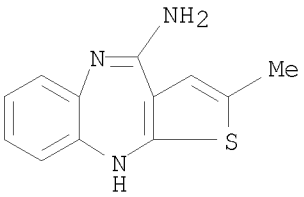
PRIORITY APPLN. INFO.:		
US 1997-60493P	P	19970930
WO 1998-US20426	W	19980930
US 2000-509757	B1	20000329
US 2002-136887	A1	20020501

AB The invention provides a pharmaceutically acceptable oleaginous or cholesterol microsphere formulation of 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2.3-b][1.5]benzodiazepine (olanzapine) (preparation given) or olanzapine pamoate or solvates thereof. The invention further provides novel olanzapine pamoate salts or solvates thereof.

IT 138564-60-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate in preparation of olanzapine)

RN 138564-60-0 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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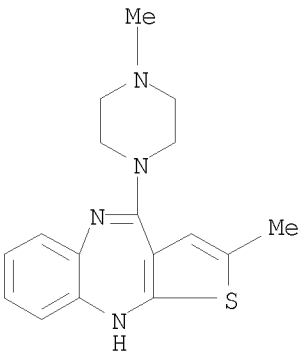
IT 132539-06-1P, Olanzapine
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and formulation of)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 33 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:233761 CAPLUS
DOCUMENT NUMBER: 130:276761
TITLE: Method for treating sexual dysfunction using 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5] benzodiazepine
INVENTOR(S): Van Tran, Pierre
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

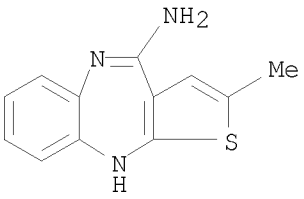
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9916312	A1	19990408	WO 1998-US20152	19980925
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2304472	A1	19990408	CA 1998-2304472	19980925
AU 9895834	A	19990423	AU 1998-95834	19980925
JP 2001517684	T	20011009	JP 2000-513466	19980925
ZA 9808840	A	20000328	ZA 1998-8840	19980928
US 20020040021	A1	20020404	US 1998-162311	19980928
US 6432943	B1	20020813		
EP 911028	A2	19990428	EP 1998-307950	19980930
EP 911028	A3	19990506		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1997-60415P P 19970930
WO 1998-US20152 W 19980925

AB The invention provides a method for treating a sexual dysfunction comprising administering an effective amount of 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5] benzodiazepine. Preparation of the compound of the invention is described, and pharmaceutical compns. are included.

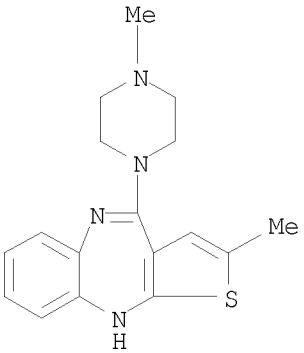
IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; thienobenzodiazepine derivative for sexual dysfunction treatment, preparation, and compns.)

RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



HCl

IT 132539-06-1D, form I
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FMU (Formation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(thienobenzodiazepine derivative for sexual dysfunction treatment, preparation,
and compns.)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-
(CA INDEX NAME)



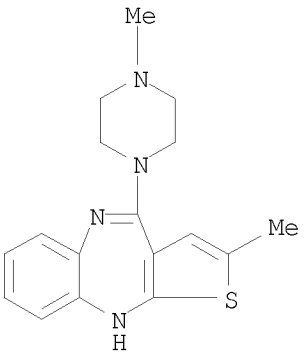
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thienobenzodiazepine deriv. for sexual dysfunction treatment, prepn., and compns.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 34 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:18019 CAPLUS
DOCUMENT NUMBER: 130:217570
TITLE: Characterization of olanzapine (LY170053) in human liver slices by liquid chromatography/tandem mass spectrometry
AUTHOR(S): Murphy, A. T.; Lake, B. G.; Bernstein, J. R.; Franklin, R. B.; Gillespie, T. A.
CORPORATE SOURCE: Department of Drug Metabolism and Disposition, Lilly Research Laboratories, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, 46285, USA
SOURCE: Journal of Mass Spectrometry (1998), 33(12), 1237-1245
CODEN: JMSPFJ; ISSN: 1076-5174
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

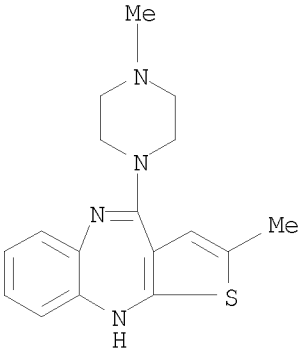
AB Olanzapine metabolism was investigated by incubation with human liver slices. Olanzapine metabolites were identified to determine if the human liver slice incubations could potentially produce quantities of the olanzapine glucuronides for future studies. Along with known Phase 1 olanzapine metabolites (N-demethyl-, 2-hydroxymethylolanzapine, and the 4'-N-oxide), a new hydroxylated species was detected. Phase 2 metabolites detected included known N-10-glucuronides, a quaternary glucuronide and a novel glucuronide conjugate. This investigation showed the feasibility of using human liver slices to produce sufficient quantities of olanzapine glucuronides for further studies.

IT 132539-06-1, Olanzapine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(liver of humans metabolism of)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

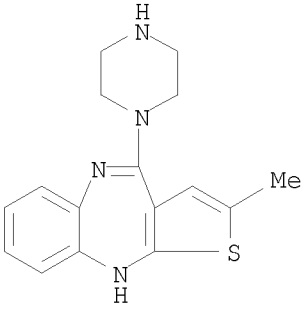


IT 132539-06-1D, Olanzapine, glucuronides 161696-76-0, LY 170055
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(olanzapine metabolism by human liver formation of)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-

(CA INDEX NAME)

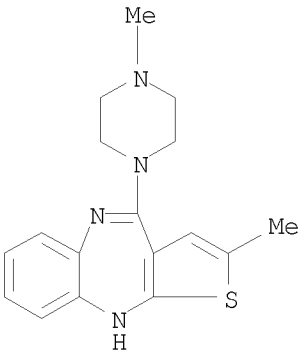


RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)

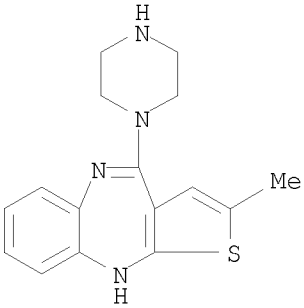


OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 35 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:787626 CAPLUS
DOCUMENT NUMBER: 130:191368
TITLE: Lack of effect of olanzapine on the pharmacokinetics of a single aminophylline dose in healthy men
AUTHOR(S): Macias, William L.; Bergstrom, Richard F.; Cerimele, Benito J.; Kassahun, Kelem; Tatum, David E.; Callaghan, John T.
CORPORATE SOURCE: Lilly Research Laboratories, and Lilly Laboratory for Clinical Research, Eli Lilly and Company, Indianapolis, IN, 46202, USA
SOURCE: Pharmacotherapy (1998), 18(6), 1237-1248
CODEN: PHPYDQ; ISSN: 0277-0008
PUBLISHER: Pharmacotherapy Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Study Objective. To test whether olanzapine, an atypical antipsychotic, is an inhibitor of cytochrome P 450 (CYP) 1A2 activity, the authors conducted a drug interaction study with theophylline, a known CYP1A2 substrate. Design. Two-way, randomized, crossover study. Setting. Clin. research laboratory Subjects. Nineteen healthy males (16 smokers, 3 nonsmokers). Interventions. Because the a priori expectation was no effect of olanzapine on theophylline pharmacokinetics, a parallel study using cimetidine was included as a pos. control. In group 1, 12 healthy subjects received a 30-min i.v. infusion of aminophylline 350 mg after 9 consecutive days of either olanzapine or placebo. In group 2, seven healthy subjects received a similar aminophylline infusion after 9 consecutive days of either cimetidine or placebo. Measurements and Main Results. Concns. of theophylline and its metabolites in serum and urine were measured for 24 and 72 h, resp. Plasma concns. of olanzapine and its metabolites were measured for 24 h after the next to last dose and 168 h after the last olanzapine dose. Olanzapine did not affect theophylline pharmacokinetics. However, cimetidine significantly decreased theophylline clearance and the corresponding formation of its metabolites. Urinary excretion of theophylline and its metabolites was unaffected by olanzapine but was reduced significantly by cimetidine. Steady-state concns. of olanzapine (15.3 ng/mL), 10-N-glucuronide (4.9 ng/mL), and 4'-N-desmethyl olanzapine (2.5 ng/mL) were observed after olanzapine 10 mg once/day and were unaffected by coadministration of theophylline. Conclusion. As predicted by in vitro studies, steady-state concns. of olanzapine and its metabolites did not affect theophylline pharmacokinetics and should not affect the pharmacokinetics of other agents metabolized by the CYP1A2 isoenzyme.
IT 132539-06-1, Olanzapine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(olanzapine does not effect pharmacokinetics of agents metabolized by CYP1A2 isoenzyme in healthy male humans)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 161696-76-0
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(olanzapine does not effect pharmacokinetics of agents metabolized by CYP1A2 isoenzyme in healthy male humans)
RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 36 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:708815 CAPLUS
DOCUMENT NUMBER: 129:335734
ORIGINAL REFERENCE NO.: 129:68341a,68344a
TITLE: Pharmaceutical compositions containing olanzapine for treatment of amyotrophic lateral sclerosis
INVENTOR(S): Bymaster, Franklin Porter; Tollefson, Gary Dennis
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

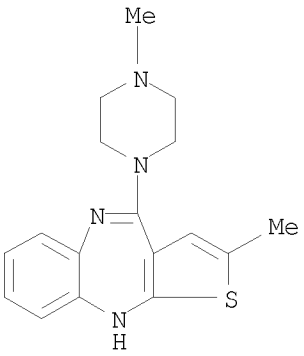
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9846596	A1	19981022	WO 1998-US6932	19980408
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9869559	A	19981111	AU 1998-69559	19980408
EP 872238	A2	19981021	EP 1998-302789	19980409
EP 872238	A3	19981028		
EP 872238	B1	20020306		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1155696	A2	20011121	EP 2001-202986	19980409
EP 1155696	A3	20020522		
EP 1155696	B1	20040303		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI, RO				
AT 213945	T	20020315	AT 1998-302789	19980409
ES 2173550	T3	20021016	ES 1998-302789	19980409
AT 260662	T	20040315	AT 2001-202986	19980409
PT 1155696	T	20040630	PT 2001-202986	19980409
ES 2215851	T3	20041016	ES 2001-202986	19980409
US 20030022889	A1	20030130	US 2002-228618	20020827

PRIORITY APPLN. INFO.:	US 1997-43094P	P	19970415
	WO 1998-US6932	W	19980408
	EP 1998-302789	A3	19980409
	US 2000-485360	B3	20000821

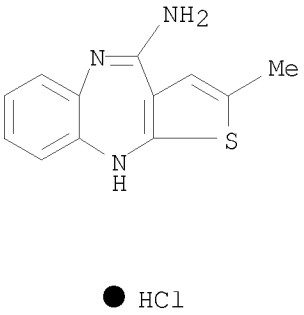
AB Pharmaceutical compns. for treating amyotrophic lateral sclerosis and for providing a neuro-protective effect comprise administering a therapeutically effective of olanzapine (I) or a pharmaceutically acceptable salt or solvate thereof. A suspension of I (preparation given) in Et acetate was heated at 76° for 30 min., then it was allowed to cool to 25°. Form II I which was isolated by filtration had potency ≥97%. Formulation of a tablet containing I was given.

IT 132539-06-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. containing olanzapine for treatment of amyotrophic

lateral sclerosis)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-
(CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(pharmaceutical compns. containing olanzapine for treatment of amyotrophic lateral sclerosis)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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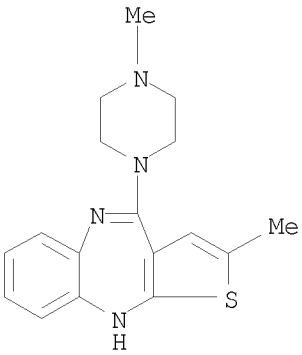
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

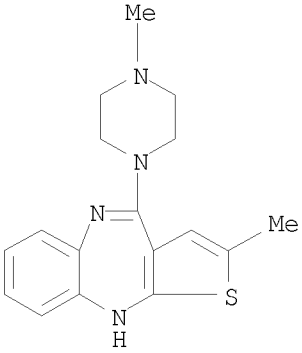
L31 ANSWER 37 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:706091 CAPLUS
DOCUMENT NUMBER: 129:298403
ORIGINAL REFERENCE NO.: 129:60729a
TITLE: Method for treating cerebral focal stroke with olanzapine
INVENTOR(S): Bymaster, Franklin Porter; Tollefson, Gary Dennis
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9846230	A1	19981022	WO 1998-US7154	19980408
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9802917	A	19991006	ZA 1998-2917	19980406
AU 9868961	A	19981111	AU 1998-68961	19980408
EP 872239	A2	19981021	EP 1998-302794	19980409
EP 872239	A3	19981028		
EP 872239	B1	20010613		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
ES 2158647	T3	20010901	ES 1998-302794	19980409
GR 3036260	T3	20011031	GR 2001-401109	20010724
PRIORITY APPLN. INFO.:			US 1997-43095P P	19970415
			WO 1998-US7154 W	19980408

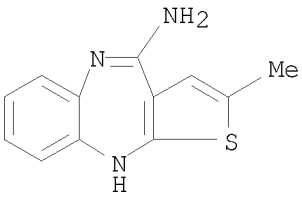
AB A method is provided for treating cerebral focal stroke comprising administering a therapeutically effective dosage of olanzapine or a pharmaceutically acceptable salt or solvate thereof. Preparation of form II olanzapine polymorph is described.
IT 132539-06-1DP, Olanzapine, form II polymorph
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(olanzapine for cerebral focal stroke treatment)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 132539-06-1P, Olanzapine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(olanzapine for cerebral focal stroke treatment)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; olanzapine for cerebral focal stroke treatment)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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OS.CITING REF COUNT:	1	THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT:	8	THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 38 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:653544 CAPLUS
DOCUMENT NUMBER: 129:286009
ORIGINAL REFERENCE NO.: 129:58149a,58152a
TITLE: 2-Methyl-4-(4-methyl-1-piperazinyl)-10H-thieno-[2,3-b][1,5]benzodiazepine for treatment of psychoactive substance disorders
INVENTOR(S): Beasley, Charles M., Jr.; Chakrabarti, Jiban Kumar; Hotten, Terrence Michael; Tupper, David Edward
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Eli Lilly and Company Limited
SOURCE: U.S., 10 pp., Cont.-in-part of U.S. 5,605,897. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

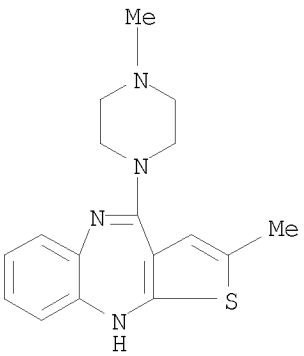
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5817657	A	19981006	US 1996-748294	19961113
US 5229382	A	19930720	US 1992-890348	19920522
US 5605897	A	19970225	US 1995-387498	19950213

PRIORITY APPLN. INFO.:
US 1991-690143 A1 19910423
US 1992-890348 A2 19920522
US 1993-44844 B2 19930408
US 1995-387498 A2 19950213
GB 1990-9229 A 19900425

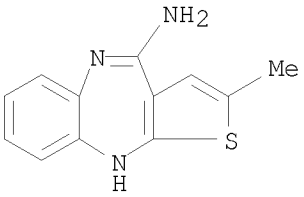
AB 2-Methyl-4-(4-methyl-1-piperazinyl)-10H-thieno-[2,3-b][1,5]benzodiazepine (preparation described), or an acid salt thereof, has pharmaceutical properties, and is of particular use in the treatment of disorders relating to the use of psychoactive substances.

IT 132539-06-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methyl(methylpiperazinyl)thienobenzodiazepine, preparation, pharmaceutical formulations, and treatment of psychoactive substance disorders)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; methyl(methylpiperazinyl)thienobenzodiazepine, preparation, pharmaceutical formulations, and treatment of psychoactive substance disorders)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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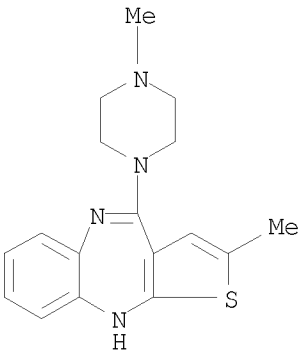
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 39 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:653543 CAPLUS
DOCUMENT NUMBER: 129:286008
ORIGINAL REFERENCE NO.: 129:58149a,58152a
TITLE: 2-Methyl-4-(4-methyl-1-piperazinyl)-10H-thieno-[2,3-b][1,5]benzodiazepine for treatment of mental disorders
INVENTOR(S): Beasley, Charles M., Jr.; Chakrabarti, Jiban Kumar; Hotten, Terrence Michael; Tupper, David Edward
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Eli Lilly and Company Limited
SOURCE: U.S., 10 pp., Cont.-in-part of U.S. 5,605,897. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5817656	A	19981006	US 1996-748293	19961113
US 5229382	A	19930720	US 1992-890348	19920522
US 5605897	A	19970225	US 1995-387498	19950213
PRIORITY APPLN. INFO.:			US 1991-690143	B1 19910423
			US 1992-890348	A2 19920522
			US 1993-44844	B2 19930408
			US 1995-387498	A2 19950213
			GB 1990-9229	A 19900425

AB 2-Methyl-4-(4-methyl-1-piperazinyl)-10H-thieno-[2,3-b][1,5]benzodiazepine (preparation described), or an acid salt thereof, has pharmaceutical properties, and is of particular use in the treatment of mental disorders.
IT 132539-06-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methyl(methylpiperazinyl)thienobenzodiazepine, preparation, pharmaceutical formulations, and use for treatment of mental disorders)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

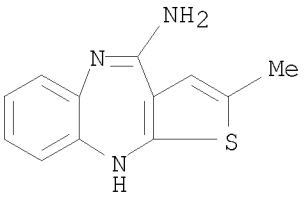


IT 138564-60-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; methyl(methylpiperazinyl)thienobenzodiazepine, preparation, pharmaceutical formulations, and use for treatment of mental disorders)

RN 138564-60-0 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

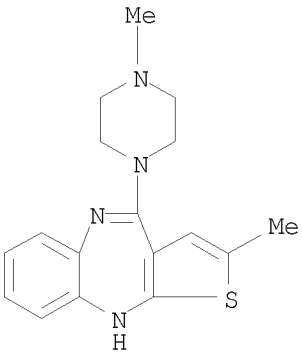
L31 ANSWER 40 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:653542 CAPLUS
DOCUMENT NUMBER: 129:270629
ORIGINAL REFERENCE NO.: 129:55025a,55028a
TITLE: Methods of treatment of psychotic conditions using a thieno-benzodiazepine
INVENTOR(S): Chakrabarti, Jiban Kumar; Hotten, Terrence Micharl; Tupper, David Edward
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; ELI LILLY AND COMPANY LIMITED
SOURCE: U.S., 10 pp., Cont.-in-part of U.S. 5,627,178.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5817655	A	19981006	US 1996-748292	19961113
US 5229382	A	19930720	US 1992-890348	19920522
US 5627178	A	19970506	US 1995-387997	19950213
US 6008216	A	19991228	US 1998-122294	19980724
US 40033	E1	20080122	US 2001-23132	20011218

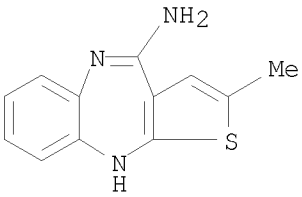
PRIORITY APPLN. INFO.:

US 1991-690143	B1	19910423
US 1992-890348	A2	19920522
US 1993-44844	B2	19930408
US 1995-387997	A2	19950213
GB 1990-9229	A	19900425
US 1996-748292	A3	19961113
US 1998-122294	E	19980724

AB 2-Methyl-4-(4-methyl-1-piperazinyl)-10H-thieno-[2,3-b][1,5]benzodiazepine (I), or an acid salt thereof, has pharmaceutical properties, and is of particular use in the treatment of disorders of the central nervous system. The results of pharmacol. tests show that I (preparation given) is an antagonist of dopamine at D-1 and D-2 receptors, has antimuscarinic anticholinergic properties, and antagonist activity at 5HT-2 receptor sites. It also has antagonist activity at noradrenergic α-receptors. Overall in clin. situations, I showed marked superiority and a better side effects profile than prior art antipsychotic agents, and had a highly advantageous activity level.
IT 132539-06-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of psychotic conditions using thieno-benzodiazepine compound)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

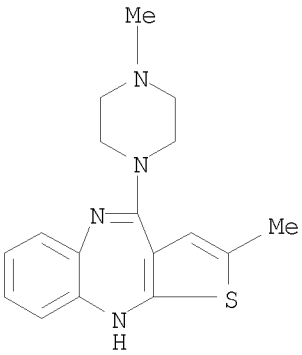


IT 138564-60-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(treatment of psychotic conditions using thieno-benzodiazepine compound)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

IT 132539-06-1D, acid addition salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of psychotic conditions using thieno-benzodiazepine compound)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

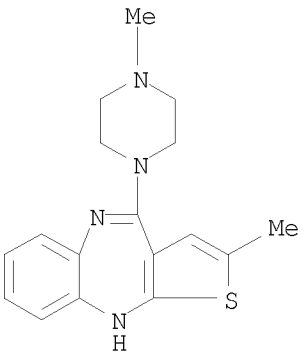


OS.CITING REF COUNT:	2	THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT:	14	THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 41 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:635108 CAPLUS
DOCUMENT NUMBER: 130:138
TITLE: Olanzapine 10-N-glucuronide; a tertiary N-glucuronide unique to humans
AUTHOR(S): Kassahun, Kelem; Mattiuz, Edward; Franklin, Ronald; Gillespie, Todd
CORPORATE SOURCE: Department of Drug Disposition, Lilly Research Laboratories, West Point, PA, 19486-0004, USA
SOURCE: Drug Metabolism and Disposition (1998), 26(9), 848-855
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

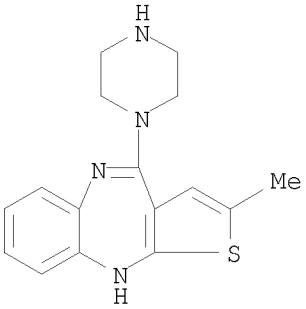
AB In humans, a major metabolite of the atypical antipsychotic olanzapine in the plasma and in the urine was an N-glucuronide. Unexpectedly, the glucuronic acid moiety was linked through a nitrogen of the benzodiazepine nucleus of olanzapine by way of a secondary amine linkage, rather than through a nitrogen on the piperazine substituent of the nucleus, to give a quaternary ammonium glucuronide. Derivatization with phenylisothiocyanate to yield a thiourea adduct indicated that conjugation occurred via a secondary amine. Subsequently, mass spectrometry and NMR studies with the isolated metabolite and later with the synthesized metabolite indicated that the glucuronide was linked at the 10- position of olanzapine. This phase 2 metabolite was only detected in the plasma and urine of human subjects and not in mice, rats, or monkeys; a trace of this metabolite was detected in dog urine. The N-10 glucuronide was resistant to enzymic and base hydrolysis but was cleaved under acidic conditions. Formation of an N-glucuronide metabolite directly with the benzodiazepine nucleus has not previously been reported.

IT 132539-06-1, Olanzapine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(olanzapine glucuronide as tertiary N-glucuronide unique to humans)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 161696-76-0, 4'-Desmethylolanzapine
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(olanzapine glucuronide as tertiary N-glucuronide unique to humans)

RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



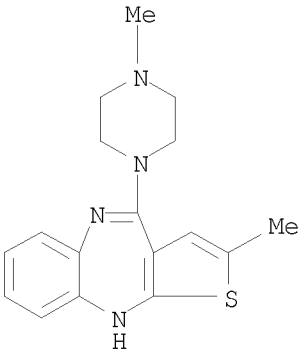
OS.CITING REF COUNT:	18	THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)
REFERENCE COUNT:	11	THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 42 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:263237 CAPLUS
DOCUMENT NUMBER: 128:312930
ORIGINAL REFERENCE NO.: 128:61929a,61932a
TITLE: Olanzapine for treating insomnia
INVENTOR(S): Van Tran, Pierre
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

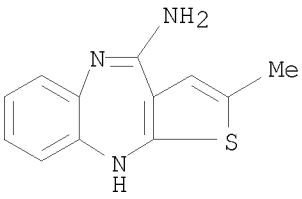
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5744470	A	19980428	US 1997-799052	19970210
PRIORITY APPLN. INFO.:			US 1997-799052	19970210

AB The invention provides a method for treating insomnia comprising administering an effective amount of olanzapine to an elderly patient who has been previously treated with a hypnotic agent. 2-Methyl-10H-thieno[2,3-b][1,5]benzodiazepin-4-amine·HCl was treated with N-methylpiperazine to obtain olanzapine, which was suspended in anhydrous EtOAc while heating and the product was isolated using vacuum filtration. The product was identified as Form II using x-ray powder anal. A tablet was formulated containing 1.18 % olanzapine.

IT 132539-06-1P, Olanzapine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(olanzapine for treating insomnia)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(olanzapine for treating insomnia)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

OS.CITING REF COUNT:	3	THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT:	2	THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 43 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:263236 CAPLUS
DOCUMENT NUMBER: 129:8586
ORIGINAL REFERENCE NO.: 129:1849a,1852a
TITLE: Method for treating dermatitis
INVENTOR(S): Tran, Pierre V.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

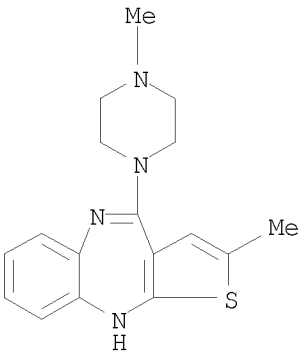
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5744469	A	19980428	US 1996-756996	19961126

PRIORITY APPLN. INFO.: US 1996-756996 19961126

AB The invention provides a method for treating fungal dermatitis comprising administering an effective amount of 2-Methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine (I) to a patient in need thereof. I was prepared from 2-methyl-4-amino-10H-thieno[2,3-b][1,5]benzodiazepine-HCl and N-methylpiperazine. Tablets containing I were prepared

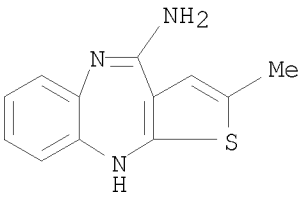
IT 132539-06-1P
RL: PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(piperazinyl thienobenzodiazepine derivative for fungal dermatitis treatment)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(piperazinyl thienobenzodiazepine derivative for fungal dermatitis treatment)

RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

OS.CITING REF COUNT:	4	THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT:	1	THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 44 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:204464 CAPLUS
DOCUMENT NUMBER: 128:275100
ORIGINAL REFERENCE NO.: 128:54369a,54372a
TITLE: Intermediates and process for preparing olanzapine
INVENTOR(S): Bunnell, Charles Arthur; Larsen, Samuel Dean; Nichols, John Richard; Reutzel, Susan Marie; Stephenson, Gregory Alan
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 831098	A2	19980325	EP 1997-307383	19970922
EP 831098	A3	19980429		
EP 831098	B1	20011121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
ZA 9708515	A	19990323	ZA 1997-8515	19970902
CA 2265712	A1	19980326	CA 1997-2265712	19970918
CA 2265712	C	20061031		
WO 9812199	A1	19980326	WO 1997-US16499	19970918
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9744841	A	19980414	AU 1997-44841	19970918
AU 719441	B2	20000511		
BR 9712100	A	19990831	BR 1997-12100	19970918
CN 1234802	A	19991110	CN 1997-198137	19970918
CN 1122036	C	20030924		
HU 2000000066	A2	20000628	HU 2000-66	19970918
HU 2000000066	A3	20001128		
HU 226484	B1	20090302		
NZ 334448	A	20000825	NZ 1997-334448	19970918
JP 2001500877	T	20010123	JP 1998-514842	19970918
IL 128962	A	20030112	IL 1997-128962	19970918
PL 194565	B1	20070629	PL 1997-332482	19970918
PL 196069	B1	20071231	PL 1997-381478	19970918
PL 196068	B1	20071231	PL 1997-381479	19970918
CZ 299248	B6	20080528	CZ 1999-990	19970918
IN 187156	A1	20020216	IN 1997-CA1736	19970919
AT 209208	T	20011215	AT 1997-307383	19970922
ES 2166051	T3	20020401	ES 1997-307383	19970922
US 6020487	A	20000201	US 1997-935884	19970923
EG 23861	A	20071118	EG 1997-986	19970923
TW 470746	B	20020101	TW 1997-86113832	19980227
HK 1009807	A1	20020913	HK 1998-110796	19980921
NO 9901382	A	19990322	NO 1999-1382	19990322
NO 323980	B1	20070730		

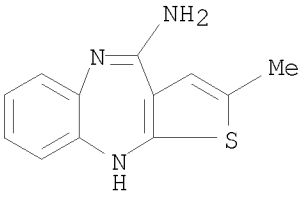
KR 2000048520	A	20000725	KR 1999-702424		19990322
JP 2009242407	A	20091022	JP 2009-135901		20090605
PRIORITY APPLN. INFO.:			US 1996-26487P	P	19960923
			JP 1998-514842	A3	19970918
			WO 1997-US16499	W	19970918

AB The present invention provides a process for preparing olanzapine and dihydrate polymorphs. Olanzapine was prepared from a known intermediate and later converted to its dihydrate. The x-ray powder anal. of the compound was carried out.

IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(intermediates and process for preparing olanzapine)

RN 138564-60-0 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)

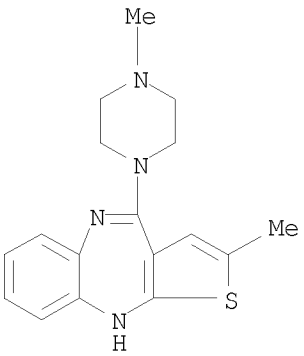


● HCl

IT 132539-06-1P, Olanzapine
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(intermediates and process for preparing olanzapine)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

L31 ANSWER 45 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:650271 CAPLUS
DOCUMENT NUMBER: 127:298752
ORIGINAL REFERENCE NO.: 127:58294h,58295a
TITLE: Olanzapine for treatment of pain
INVENTOR(S): Helton, David R.; Kallman, Mary J.; Shannon, Harlan E.; Womer, Daniel E.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

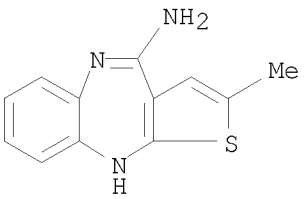
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9735583	A1	19971002	WO 1997-US4626		19970324
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU					
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2248873	A1	19971002	CA 1997-2248873		19970324
AU 9723408	A	19971017	AU 1997-23408		19970324
AU 721338	B2	20000629			
EP 910381	A1	19990428	EP 1997-916159		19970324
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
CN 1219878	A	19990616	CN 1997-194952		19970324
BR 9708246	A	19990727	BR 1997-8246		19970324
HU 9902723	A2	20000228	HU 1999-2723		19970324
HU 9902723	A3	20000428			
HU 9903183	A2	20000228	HU 1999-3183		19970324
HU 9903183	A3	20011228			
US 6258807	B1	20010710	US 1997-823460		19970324
JP 2001517202	T	20011002	JP 1997-534509		19970324
NO 9804446	A	19981125	NO 1998-4446		19980924
KR 2000004964	A	20000125	KR 1998-707568		19980924
PRIORITY APPLN. INFO.:			US 1996-14131P	P	19960325
			US 1996-14133P	P	19960325
			US 1996-14153P	P	19960325
			WO 1997-US4626	W	19970324

AB The present invention provides a method for treating pain comprising administering an analgesic dosage of olanzapine or its polymorph. Olanzapine was prepared by reaction of 2-methyl-4-amino-10H-thieno[2,3-b][1,5]-benzodiazepine with N-methylpiperazine in DMSO. Olanzapine tablets were prepared by using a coating solution of 10% HPMC.

IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(analgesic compns. containing olanzapine)

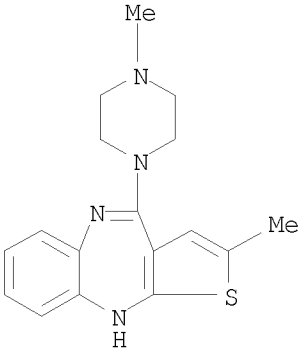
RN 138564-60-0 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

IT 132539-06-1P, Olanzapine
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(analgesic compns. containing olanzapine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 46 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:650270 CAPLUS
DOCUMENT NUMBER: 127:298751
ORIGINAL REFERENCE NO.: 127:58291a,58294a
TITLE: Method for treating migraine pain
INVENTOR(S): Shannon, Harlan E.; Womer, Daniel E.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

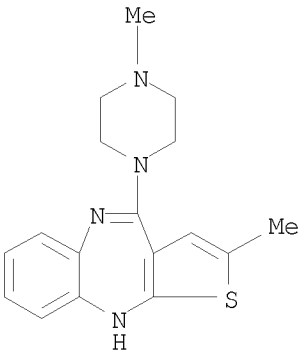
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9735582	A1	19971002	WO 1997-US4471	19970324
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2250186	A1	19971002	CA 1997-2250186	19970324
AU 9725845	A	19971017	AU 1997-25845	19970324
AU 721290	B2	20000629		
CN 1219876	A	19990616	CN 1997-194950	19970324
CN 1106196	C	20030423		
BR 9708145	A	19990727	BR 1997-8145	19970324
US 5929070	A	19990727	US 1997-823457	19970324
EP 932407	A1	19990804	EP 1997-917556	19970324
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
NZ 332037	A	20010126	NZ 1997-332037	19970324
JP 2001508759	T	20010703	JP 1997-534491	19970324
IL 126063	A	20020421	IL 1997-126063	19970324
NO 9804432	A	19981124	NO 1998-4432	19980923
KR 2000004966	A	20000125	KR 1998-707570	19980924
PRIORITY APPLN. INFO.:			US 1996-14127P P	19960325
			WO 1997-US4471 W	19970324

AB The present invention provides a method for treating migraine pain comprising administering an analgesic dosage of olanzapine. Olanzapine was prepared and a polymorphic form prepared and characterized. Tablet formulations were given.

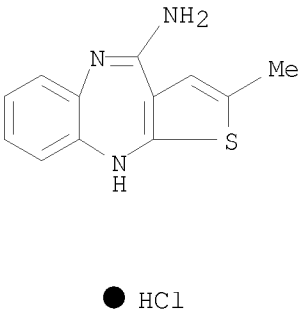
IT 132539-06-1P, Olanzapine
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(olanzapine compns. for treatment of migraine pain)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0, 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, monohydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(olanzapine compns. for treatment of migraine pain)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 47 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:632496 CAPLUS
DOCUMENT NUMBER: 127:268052
ORIGINAL REFERENCE NO.: 127:52223a
TITLE: Olanzapine for the treatment of insomnia
INVENTOR(S): Van Tran, Pierre
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

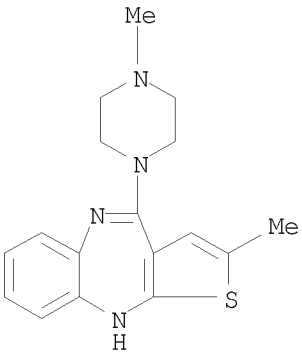
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 795330	A1	19970917	EP 1997-301534		19970307
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
ZA 9701899	A	19980907	ZA 1997-1899		19970305
CA 2248758	A1	19970918	CA 1997-2248758		19970307
WO 9733587	A1	19970918	WO 1997-US3592		19970307
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, YU					
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9721989	A	19971001	AU 1997-21989		19970307
AU 724245	B2	20000914			
CN 1212627	A	19990331	CN 1997-192796		19970307
BR 9708181	A	19990727	BR 1997-8181		19970307
JP 2000506528	T	20000530	JP 1997-532707		19970307
NZ 331846	A	20000728	NZ 1997-331846		19970307
NO 9804190	A	19980911	NO 1998-4190		19980911
PRIORITY APPLN. INFO.:			US 1996-13126P	P	19960311
			GB 1996-6731	A	19960329
			WO 1997-US3592	W	19970307

AB The invention discloses the use of olanzapine for treating insomnia. The preparation and polymorphic form of olanzapine were given and tablets were prepared

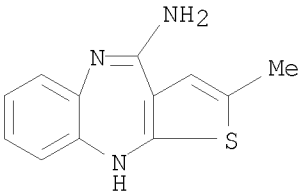
IT 132539-06-1P, Olanzapine
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(olanzapine for the treatment of insomnia)

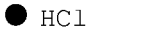
RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(olanzapine for the treatment of insomnia)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)





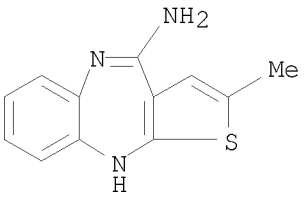
L31 ANSWER 48 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:623040 CAPLUS
DOCUMENT NUMBER: 127:268044
ORIGINAL REFERENCE NO.: 127:52219a,52222a
TITLE: Olanzapine for treating autism and mental retardation
INVENTOR(S): Beasley, Charles M., Jr.; Tollefson, Gary D.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Beasley, Charles M. Jr.; Tollefson, Gary D.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9733585	A1	19970918	WO 1996-US19576		19961204
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2248741	A1	19970918	CA 1996-2248741		19961204
AU 9711501	A	19971001	AU 1997-11501		19961204
AU 709181	B2	19990826			
CN 1213970	A	19990414	CN 1996-180207		19961204
BR 9612552	A	19990720	BR 1996-12552		19961204
EP 946179	A1	19991006	EP 1996-942934		19961204
EP 946179	B1	20030917			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI					
HU 9903688	A2	20000328	HU 1999-3688		19961204
HU 9903688	A3	20011228			
JP 2000506860	T	20000606	JP 1997-532571		19961204
NZ 324615	A	20000825	NZ 1996-324615		19961204
AT 249832	T	20031015	AT 1996-942934		19961204
ES 2206614	T3	20040516	ES 1996-942934		19961204
NO 9804197	A	19981103	NO 1998-4197		19980911
PRIORITY APPLN. INFO.:			US 1996-13162P	P	19960311
			WO 1996-US19576	W	19961204

AB The invention provides a method for treating autistic disorder and/or mental retardation comprising administering an effective amount of olanzapine (I) to a patient in need thereof. I is preferably in Form II polymorph and orally administered. I was suspended in anhydrous EtOAc, heated to 76°, cooled to 25°, and isolated using vacuum filtration. The product was identified as Form II using x-ray powder anal. I was formulated into tablets.

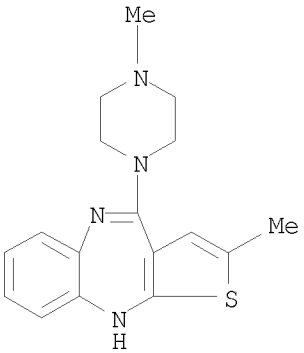
IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(olanzapine for treating autism and mental retardation)

RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

IT 132539-06-1P, Olanzapine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(olanzapine for treating autism and metal retardation)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 49 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:623039 CAPLUS
DOCUMENT NUMBER: 127:268043
ORIGINAL REFERENCE NO.: 127:52219a,52222a
TITLE: Olanzapine for treating excessive aggression
INVENTOR(S): Beasley, Charles M., Jr.; Tran, Pierre V.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Beasley, Charles M., Jr.; Tran, Pierre V.
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

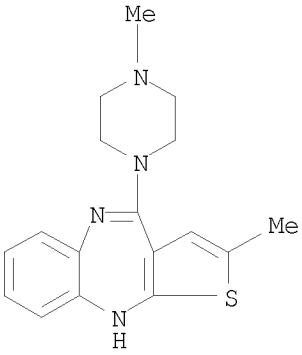
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9733584	A1	19970918	WO 1996-US19573	19961204
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2248753	A1	19970918	CA 1996-2248753	19961204
CA 2248753	C	20081118		
AU 9712846	A	19971001	AU 1997-12846	19961204
AU 719517	B2	20000511		
EP 900085	A1	19990310	EP 1996-943659	19961204
EP 900085	B1	20051012		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1213969	A	19990414	CN 1996-180206	19961204
CN 1124847	C	20031022		
BR 9612549	A	19990720	BR 1996-12549	19961204
HU 9903685	A2	20000328	HU 1999-3685	19961204
HU 9903685	A3	20011228		
JP 2000506858	T	20000606	JP 1997-532569	19961204
NZ 325035	A	20010629	NZ 1996-325035	19961204
RO 117347	B1	20020228	RO 1998-1386	19961204
IL 126157	A	20020912	IL 1996-126157	19961204
PL 186975	B1	20040430	PL 1996-328949	19961204
AT 306269	T	20051015	AT 1996-943659	19961204
ES 2249789	T3	20060401	ES 1996-943659	19961204
CZ 296579	B6	20060412	CZ 1998-2905	19961204
NO 9804198	A	19981102	NO 1998-4198	19980911
NO 323579	B1	20070611		

PRIORITY APPLN. INFO.: US 1996-13127P P 19960311
WO 1996-US19573 W 19961204

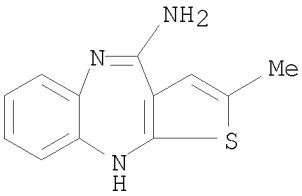
AB The invention provides a method for treating extreme aggression comprising administering an effective amount of olanzapine to a patient in need thereof.

IT 132539-06-1, Olanzapine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC

(Process); USES (Uses)
(crystal polymorph II; olanzapine for treating excessive aggression)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-
(CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(olanzapine for treating excessive aggression)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride
(1:1) (CA INDEX NAME)

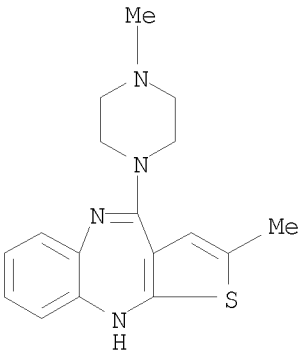


OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

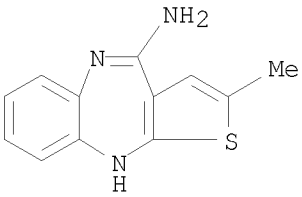
L31 ANSWER 50 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:503273 CAPLUS
DOCUMENT NUMBER: 127:126642
ORIGINAL REFERENCE NO.: 127:24313a,24316a
TITLE: Method for treating depression
INVENTOR(S): Tollefson, Gary D.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Tollefson, Gary D.
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9723220	A1	19970703	WO 1996-US19574	19961204
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2241153	A1	19970703	CA 1996-2241153	19961204
AU 9712847	A	19970717	AU 1997-12847	19961204
AU 705834	B2	19990603		
EP 868185	A1	19981007	EP 1996-943660	19961204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
CN 1205637	A	19990120	CN 1996-199221	19961204
HU 9903684	A2	20000328	HU 1999-3684	19961204
HU 9903684	A3	20011228		
NZ 325036	A	20010629	NZ 1996-325036	19961204
US 5958921	A	19990928	US 1998-91539	19980618
PRIORITY APPLN. INFO.:			US 1995-9173P P	19951222
			WO 1996-US19574 W	19961204

AB The invention provides a method for treating depressive signs and symptoms comprising administering an effective amount of 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine to a patient in need thereof.
IT 132539-06-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and antidepressant activity of methyl(methylpiperazinyl)thienobenzodiazepine and tablet formulation)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and antidepressant activity of
methyl(methylpiperazinyl)thienobenzodiazepine and tablet formulation)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride
(1:1) (CA INDEX NAME)



● HCl

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 51 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:503266 CAPLUS
DOCUMENT NUMBER: 127:117375
ORIGINAL REFERENCE NO.: 127:22505a,22508a
TITLE: 2-Methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine for treating fungal dermatitis
INVENTOR(S): Tran, Pierre V.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Tran, Pierre V.
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

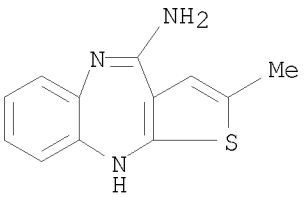
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9723221	A1	19970703	WO 1996-US20048	19961216
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2240836	A1	19970703	CA 1996-2240836	19961216
AU 9713353	A	19970717	AU 1997-13353	19961216
JP 2000502346	T	20000229	JP 1997-523755	19961216
EP 783890	A1	19970716	EP 1996-309201	19961217
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				

PRIORITY APPLN. INFO.: US 1995-8987P P 19951221
WO 1996-US20048 W 19961216

AB A method for treating fungal dermatitis comprises administering an effective amount of 2-Methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine (I) to a patient in need thereof. The effectiveness of I was shown in a clin. trial. Preparation of I is described. A tablet formulation is included.

IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; thienobenzodiazepine derivative for fungal dermatitis treatment)

RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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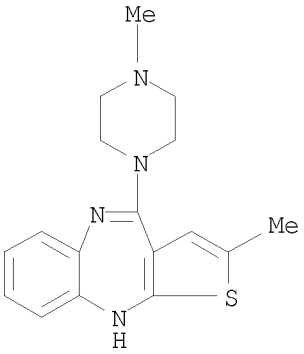
IT 132539-06-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thienobenzodiazepine derivative for fungal dermatitis treatment)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 52 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:403057 CAPLUS
DOCUMENT NUMBER: 127:13469
ORIGINAL REFERENCE NO.: 127:2623a,2626a
TITLE: Olanzapine for treatment of obsessive-compulsive disorder
INVENTOR(S): Beasley, Charles Merritt, Jr.; Tollefson, Gary Dennis
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Brit. UK Pat. Appl., 18 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

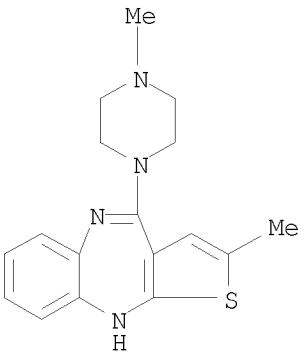
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2305859	A	19970423	GB 1996-6614	19960329

PRIORITY APPLN. INFO.: GB 1996-6614 19960329

AB Olanzapine is useful in the treatment of obsessive-compulsive disorder. The olanzapine may be the form II olanzapine polymorph. Preparation of the polymorph is described. Preparation of a tablet formulation is also included.

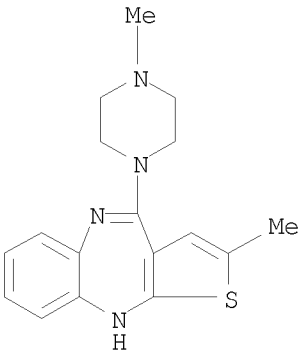
IT 132539-06-1, Olanzapine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(olanzapine for treatment of obsessive-compulsive disorder)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

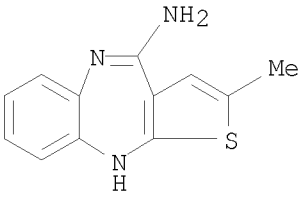


IT 132539-06-1D, Olanzapine, form II polymorph
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(olanzapine polymorph for treatment of obsessive-compulsive disorder)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; olanzapine for treatment of obsessive-compulsive disorder)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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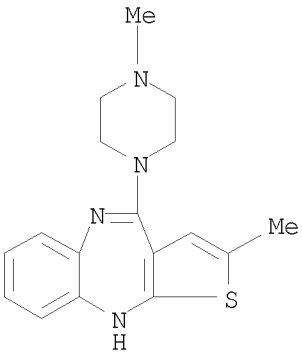
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

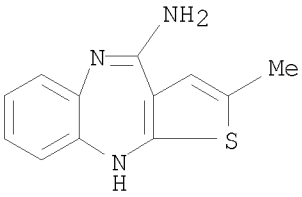
L31 ANSWER 53 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:332391 CAPLUS
DOCUMENT NUMBER: 126:308810
ORIGINAL REFERENCE NO.: 126:59765a,59768a
TITLE: Pharmaceutical compositions for treating a tic disorder
INVENTOR(S): Beasley, Charles M., Jr.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Beasley, Charles M., Jr.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9711700	A1	19970403	WO 1996-US14090	19960827
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
CA 2232559	A1	19970403	CA 1996-2232559	19960827
AU 9670131	A	19970417	AU 1996-70131	19960827
EP 852496	A1	19980715	EP 1996-931453	19960827
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11512705	T	19991102	JP 1996-513436	19960827
US 6274636	B1	20010814	US 1999-242418	19990216
PRIORITY APPLN. INFO.:			US 1995-5176P	P 19950929
			WO 1996-US14090	W 19960827

AB A pharmaceutical composition for treating a tic disorder comprise administering an effective amount of 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine (preparation given) (I). A tablet contained I 10.0, magnesium stearate 0.9, microcryst. cellulose 75.0, povidone 25.0, and starch 204.1 mg.
IT 132539-06-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. for treating tic disorder)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(pharmaceutical compns. for treating tic disorder)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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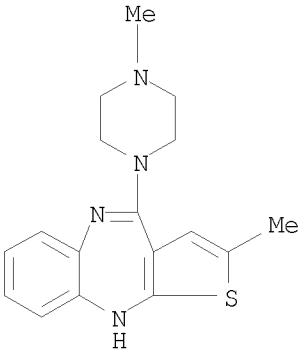
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

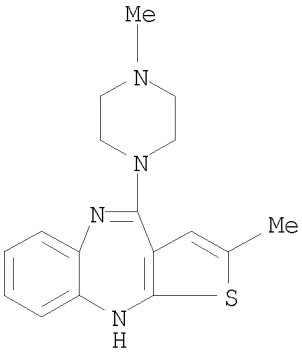
L31 ANSWER 54 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:329809 CAPLUS
DOCUMENT NUMBER: 127:60154
ORIGINAL REFERENCE NO.: 127:11313a,11316a
TITLE: Disposition and metabolism of olanzapine in mice, dogs, and rhesus monkeys
AUTHOR(S): Mattiuz, Edward; Franklin, Ronald; Gillespie, Todd; Murphy, Anthony; Bernstein, John; Chiur, Andre; Hotten, Terry; Kassahun, Kelem
CORPORATE SOURCE: Dep. Drug Metabolism, Lilly Corporate Center, Eli Lilly Company, Indianapolis, IN, 46285, USA
SOURCE: Drug Metabolism and Disposition (1997), 25(5), 573-583
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Olanzapine (OLZ) is a novel antipsychotic agent with a high affinity for serotonin (5-HT2), dopamine (D1/D2/D4), muscarinic (m1-m5), adrenergic (α1), and histamine (H1) receptors. The pharmacokinetics, excretion, and metabolism of OLZ were studied in CD-1 mice, beagles dogs, and rhesus monkeys after a single oral and/or i.v. dose of [14C]OLZ. After oral administration, OLZ was well absorbed in dogs (absolute bioavailability of 73%) and to the extent of at least 55% in monkeys and 32% in mice. The terminal elimination half-life of OLZ was relatively short in mice and monkeys, (.apprx.3 h) and long in dogs (.apprx.9 h). In mice and dogs, radioactivity was predominantly eliminated in feces; but, in monkeys, the major route of elimination of radioactivity was urine. Dogs and monkeys excreted in urine, resp., 38% and 55% of the dose over a 168-h period, whereas the fraction of the dose excreted in urine of mice over the collection period (120 h) was 32%. OLZ was subject to substantial first-pass metabolism; at the tmax, OLZ accounted for 19%, 18% and 18% of the radioactivity in mice, dogs, and monkeys, resp. The ratio of AUC OLZ to AUC radioactivity was, resp., 10%, 14%, and 4% in mice, dogs, and monkeys. The principal urinary metabolites in mice were 7-hydroxy OLZ glucuronide, 2-hydroxymethyl OLZ, and 2-carboxy OLZ accounting for .apprx.10%, 4%, and 2% of the dose. Metabolites that were present in urine in lesser amts. were 7-hydroxy OLZ, N-desmethyl OLZ, and N-desmethyl-2-hydroxymethyl OLZ. In dogs, the major metabolite accounting for .apprx.8% of the dose was 7-hydroxy-N-oxide OLZ. Other metabolites identified were 2-hydroxymethyl OLZ, 2-carboxy OLZ, N-oxide OLZ, 7-hydroxy OLZ, and its glucuronide and N-desmethyl OLZ. The major metabolite in monkey urine was N-desmethyl-2-carboxy OLZ, and accounted for .apprx.17% of the dose. In addition, N-oxide-2-hydroxymethyl OLZ, N-oxide-2-carboxy OLZ, N-desmethyl-2-hydroxymethyl, 2-carboxy OLZ, and 2-hydroxymethyl OLZ were identified in monkeys urine. Thus, in mice and dogs, OLZ was metabolized through aromatic hydroxylation, allylic oxidation, N-dealkylation, and N-oxidation reactions. In monkeys, OLZ was biotransformed mainly through double oxidation reactions involving the allylic carbon and Me piperazine nitrogen. Whereas the oxidative metabolic profile of OLZ in animals was similar to that of humans, animals were notable for not forming appreciable amts. of the principal human metabolite (i.e. 10-N-glucuronide OLZ).
IT 132539-06-1, Olanzapine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(disposition and metabolism of olanzapine in mice, dogs, and rhesus monkeys)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

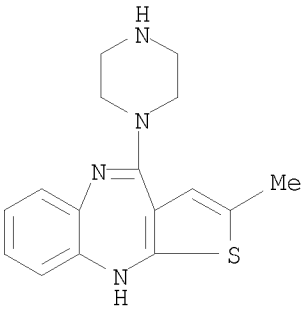


IT 132539-06-1D, Olanzapine, conjugates with N-acetylcysteine or cysteine 161696-76-0
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(disposition and metabolism of olanzapine in mice, dogs, and rhesus monkeys)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



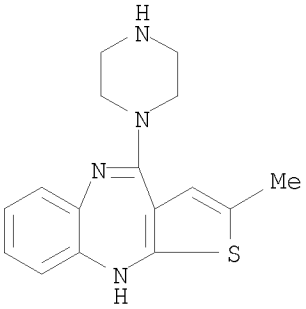
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 55 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:63851 CAPLUS
DOCUMENT NUMBER: 126:180769
ORIGINAL REFERENCE NO.: 126:34725a,34728a
TITLE: Disposition and biotransformation of the antipsychotic agent olanzapine in humans
AUTHOR(S): Kassahun, Kelem; Mattiuz, Edward; Nyhart, Eldon, Jr.; Obermeyer, Boyd; Gillespie, Todd; Murphy, Anthony; Goodwin, R. Michael; Tupper, David; Callaghan, J. Thomas; Lemberger, Louis
CORPORATE SOURCE: Department of Drug Metabolism, Lilly Research Laboratories, Eli Lilly and Company, Lilly Research Centre, Indianapolis, IN, 46285, USA
SOURCE: Drug Metabolism and Disposition (1997), 25(1), 81-93
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

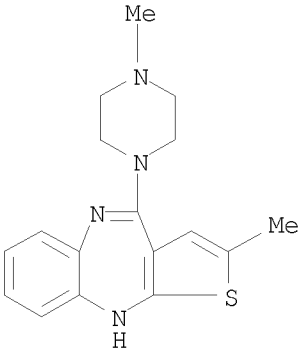
AB Disposition and biotransformation of the new antipsychotic agent olanzapine (OLZ) were studied in six male healthy volunteers after a single oral dose of 12.5 mg containing 100 μCi of [14C]OLZ. Biol. fluids were analyzed for total radioactivity, the parent compound (GC/MS), and metabolites (electrospray LC/MS and LC/MS/MS). Mean radiocarbon recovery was .apprx.87%, with 30% appearing in the feces and 57% excreted in the urine. Approx. half of the radiocarbon was excreted within 3 days, whereas >70% of the dose was recovered within 7 days of dosing. Circulating radioactivity was mostly restricted to the plasma compartment of blood. Mean peak plasma concentration of OLZ was 11 ng/mL, whereas that of radioactivity was 39 ng eq/mL. Mean plasma terminal elimination half-lives were 27 and 59 h, resp., for OLZ and total radioactivity. With the help of NMR and MS data, a major metabolite of OLZ in humans was characterized as a novel tertiary N-glucuronide in which the glucuronic acid moiety is attached to the nitrogen at position 10 of the benzodiazepine ring. Another N-glucuronide was detected in urine and identified as the quaternary N-linked 4'-N-glucuronide. Oxidative metabolism on the allylic Me group resulted in 2-hydroxymethyl and 2-carboxylic acid derivs. of OLZ. The Me piperazine moiety was also subject to oxidative attack, giving rise to the N-oxide and N-desmethyl metabolites. Other metabolites, including the N-desmethyl-2-carboxy derivative, resulted from metabolic reactions at both the 4' nitrogen and 2-Me groups. The 10-N-glucuronide and OLZ were the two most abundant urinary components, accounting for .apprx.13% and 7% of the dose, resp. In fecal exts., the only significant radioactive HPLC peaks were due to 10-N-glucuronide and OLZ representing, resp., .apprx.8% and 2% of the administered dose. Semiquant. data obtained from plasma samples from subjects given [14C]OLZ suggest that the main circulating metabolite is 10-N-glucuronide. Thus, OLZ was extensively metabolized in humans via N-glucuronidation, allylic hydroxylation, N-oxidation, N-dealkylation and a combination thereof. The 10-N-glucuronidation pathway was the most important pathway both in terms of contribution to drug-related circulating species and as an excretory product in feces and urine.

IT 161696-76-0
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(disposition and biotransformation of antipsychotic agent olanzapine in humans)

RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



IT 132539-06-1, Olanzapine
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(disposition and biotransformation of antipsychotic agent olanzapine in humans)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

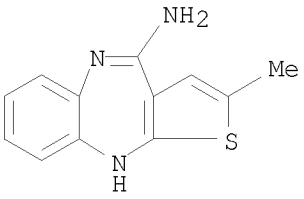


OS.CITING REF COUNT: 88 THERE ARE 88 CAPLUS RECORDS THAT CITE THIS RECORD (88 CITINGS)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 56 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:56315 CAPLUS
DOCUMENT NUMBER: 126:152692
ORIGINAL REFERENCE NO.: 126:29391a,29394a
TITLE: The synthesis and biological activity of some known and putative metabolites of the atypical antipsychotic agent olanzapine (LY170053)
AUTHOR(S): Calligaro, David O.; Fairhurst, John; Hotten, Terrence M.; Moore, Nicholas A.; Tupper, David E.
CORPORATE SOURCE: Lilly Res. Cent. Ltd., Eli Lilly Co., Surrey, GU20 6PH, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(1), 25-30
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 4'-N-desmethyl olanzapine, olanzapine 4'-N-oxide and 2-hydroxymethyl olanzapine have been prepared and their pharmacol. compared to that of the parent compound olanzapine. The 4'-N-quaternary glucuronide has also been prepared All metabolites were significantly less active than olanzapine in the tests conducted: binding to neuronal receptors, apomorphine-induced climbing behavior in mice and conditioned avoidance behavior in rats.

IT 138564-60-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; synthesis and biol. activity of known and putative metabolites of antipsychotic agent olanzapine)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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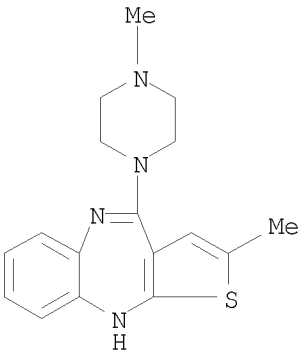
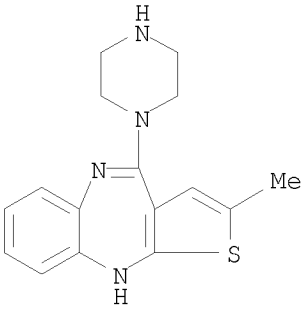
IT 132539-06-1, Olanzapine
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(synthesis and biol. activity of known and putative metabolites of antipsychotic agent olanzapine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 161696-76-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); USES (Uses)
(synthesis and biol. activity of known and putative metabolites of antipsychotic agent olanzapine)
RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 57 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:689366 CAPLUS
DOCUMENT NUMBER: 125:309062
ORIGINAL REFERENCE NO.: 125:57669a,57672a
TITLE: Olanzapine for treatment of dyskinesias
INVENTOR(S): Beasley, Charles Merrit, Jr.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 738514	A1	19961023	EP 1996-302711	19960418
EP 738514	B1	20030827		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5776928	A	19980707	US 1995-422177	19950421
CA 2219902	A1	19961205	CA 1995-2219902	19950530
WO 9638151	A1	19961205	WO 1995-US6859	19950530
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9526936	A	19961218	AU 1995-26936	19950530
AU 707858	B2	19990722		
EP 828494	A1	19980318	EP 1995-922148	19950530
EP 828494	B1	20020717		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV				
CN 1185108	A	19980617	CN 1995-197876	19950530
CN 1131035	C	20031217		
HU 77907	A2	19981028	HU 1998-1173	19950530
JP 11506096	T	19990602	JP 1995-536420	19950530
RU 2176914	C2	20011220	RU 1997-122082	19950530
AT 220550	T	20020815	AT 1995-922148	19950530
ES 2180643	T3	20030216	ES 1995-922148	19950530
CZ 292565	B6	20031015	CZ 1997-3243	19950530
PL 189714	B1	20050930	PL 1995-323785	19950530
CA 2218062	A1	19961024	CA 1996-2218062	19960418
WO 9632948	A1	19961024	WO 1996-US5390	19960418
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9655555	A	19961107	AU 1996-55555	19960418
ZA 9603098	A	19971020	ZA 1996-3098	19960418
JP 11504014	T	19990406	JP 1996-531914	19960418
IL 117971	A	19991231	IL 1996-117971	19960418
AT 247966	T	20030915	AT 1996-302711	19960418

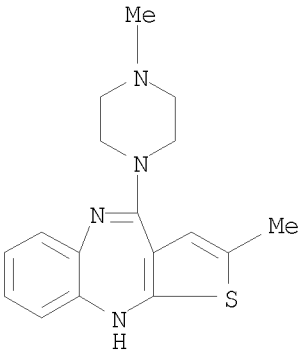
ES 2206544	T3	20040516	ES 1996-302711		19960418
NO 9704766	A	19971209	NO 1997-4766		19971015
NO 318553	B1	20050411			
FI 9703987	A	19971017	FI 1997-3987		19971017
US 20020177590	A1	20021128	US 1997-952918		19971125
US 6506746	B2	20030114			
HK 1009393	A1	20030516	HK 1998-110242		19980826
PRIORITY APPLN. INFO.:			US 1995-422177	A	19950421
			CA 1995-2219902	A	19950530
			EP 1995-922148	A	19950530
			WO 1995-US6859	W	19950530
			WO 1996-US5390	W	19960418

AB Use of 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine (olanzapine) or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating a dyskinesia, is disclosed. Oral and injection formulations are provided.

IT 132539-06-1P, Olanzapine
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(olanzapine for treatment of dyskinesias)

RN 132539-06-1 CAPLUS

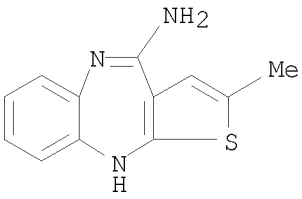
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(olanzapine for treatment of dyskinesias)

RN 138564-60-0 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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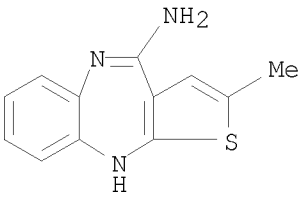
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

L31 ANSWER 58 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:679179 CAPLUS
DOCUMENT NUMBER: 125:309063
ORIGINAL REFERENCE NO.: 125:57669a,57672a
TITLE: Olanzapine for treatment of nicotine withdrawal syndromes
INVENTOR(S): Rasmussen, Kurt
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 738515	A1	19961023	EP 1996-302712	19960418
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5696115	A	19971209	US 1995-422202	19950421
CA 2218019	A1	19961024	CA 1996-2218019	19960418
WO 9632947	A1	19961024	WO 1996-US5379	19960418
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9655547	A	19961107	AU 1996-55547	19960418
ZA 9603108	A	19971020	ZA 1996-3108	19960418
JP 11504012	T	19990406	JP 1996-531909	19960418
IL 117970	A	19991222	IL 1996-117970	19960418
TW 429149	B	20010411	TW 1996-85104731	19960420
PRIORITY APPLN. INFO.:			US 1995-422202 A	19950421
			WO 1996-US5379 W	19960418

AB Use of 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine (olanzapine) or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating a condition resulting from the cessation and withdrawal from the use of nicotine, is disclosed. Formulations containing olanzapine for oral and i.m. administration, are provided.
IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(olanzapine for treatment of nicotine withdrawal syndromes)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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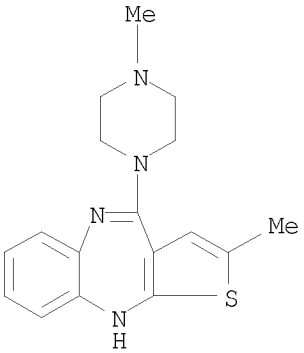
IT 132539-06-1P, Olanzapine
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(olanzapine for treatment of nicotine withdrawal syndromes)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

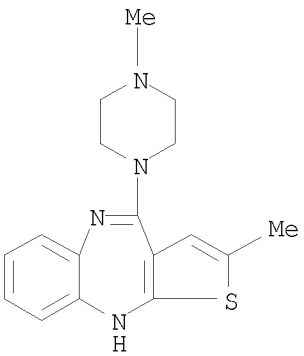
L31 ANSWER 59 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:660927 CAPLUS
DOCUMENT NUMBER: 125:284961
ORIGINAL REFERENCE NO.: 125:53125a,53128a
TITLE: Granule formulation for olanzapine
INVENTOR(S): Lange, Hans Joerg
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 733368	A1	19960925	EP 1996-301998	19960322
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
IN 1996CA00513	A	20050304	IN 1996-CA513	19960322
PRIORITY APPLN. INFO.:			US 1995-410265 A	19950324
			US 1995-426343 A	19950421

AB The invention provides a pharmaceutically elegant granule formulation of olanzapine and a process for providing a pharmaceutically acceptable liquid formulation of olanzapine. The solid granule formulation comprises olanzapine as an active ingredient, mannitol, hydroxypropyl Me cellulose, and a pharmaceutically acceptable surfactant, provided that the size of the granules is such that not more than 5% are greater than 500 μm and not more than 10% are less than 75 μm. Granules were prepared and packaged in a sachet to have ingredients of olanzapine 2.5, D-mannitol 234.97, hydroxypropyl Me cellulose 12.5, and Polysorbate 20 0.028 mg. The granules can be dissolved in an acidic mineral water or juice.

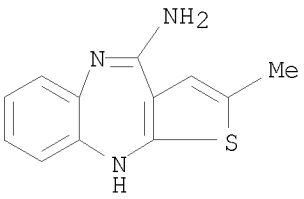
IT 132539-06-1P, Olanzapine
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(granule formulation for olanzapine)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(granule formulation for olanzapine)

RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L31 ANSWER 60 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:660926 CAPLUS
DOCUMENT NUMBER: 125:284960
ORIGINAL REFERENCE NO.: 125:53125a,53128a
TITLE: Oral olanzapine formulation
INVENTOR(S): Cochran, George Randall; Morris, Tommy Clifford
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 733367	A1	19960925	EP 1996-301997	19960322
EP 733367	B1	20011017		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EG 24077	A	20080511	EG 1996-251	19960321
CA 2216372	A1	19961003	CA 1996-2216372	19960322
CA 2216372	C	20071120		
WO 9629995	A1	19961003	WO 1996-US3918	19960322
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9654280	A	19961016	AU 1996-54280	19960322
AU 696601	B2	19980917		
ZA 9602338	A	19970922	ZA 1996-2338	19960322
GB 2313783	A	19971210	GB 1997-19817	19960322
GB 2313783	B	19981118		
DE 19681287	T0	19980319	DE 1996-19681287	19960322
CN 1179102	A	19980415	CN 1996-192778	19960322
CN 1178662	C	20041208		
BR 9607791	A	19980707	BR 1996-7791	19960322
HU 9800410	A2	19980728	HU 1998-410	19960322
HU 9800410	A3	20000128		
HU 225269	B1	20060828		
AT 9609022	A	19990215	AT 1996-9022	19960322
AT 405606	B	19991025		
JP 11502848	T	19990309	JP 1996-529533	19960322
TW 426526	B	20010321	TW 1996-85103453	19960322
EP 1093815	A1	20010425	EP 2000-204708	19960322
EP 1093815	B1	20041215		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CH 691217	A5	20010531	CH 1997-2246	19960322
AT 206924	T	20011115	AT 1996-301997	19960322
EE 3551	B1	20011217	EE 1997-328	19960322
ES 2164837	T3	20020301	ES 1996-301997	19960322
IL 117611	A	20020523	IL 1996-117611	19960322
RO 118370	B1	20030530	RO 1997-1776	19960322
SK 283745	B6	20031202	SK 1997-1282	19960322
AT 284695	T	20050115	AT 2000-204708	19960322

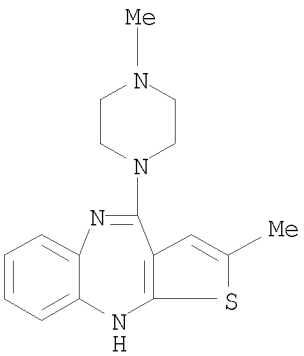
PL 188316	B1	20050131	PL 1996-322579		19960322
ES 2232379	T3	20050601	ES 2000-204708		19960322
CZ 296007	B6	20051214	CZ 1997-3001		19960322
IN 1996CA00517	A	20060113	IN 1996-CA517		19960322
SE 9703206	A	19970905	SE 1997-3206		19970905
LT 4350	B	19980525	LT 1997-149		19970916
FI 9703749	A	19970922	FI 1997-3749		19970922
NO 9704363	A	19971117	NO 1997-4363		19970922
NO 320388	B1	20051128			
DK 9701090	A	19971112	DK 1997-1090		19970923
DK 173323	B1	20000724			
LV 11983	B	19980720	LV 1997-199		19971014
IN 1999CA00416	A	20050311	IN 1999-CA416		19990504
IN 2007KO00577	A	20071026	IN 2007-KO577		20070413
PRIORITY APPLN. INFO.:			US 1995-410465	A	19950324
			EP 1996-301997	A3	19960322
			IN 1996-CA517	A3	19960322
			WO 1996-US3918	W	19960322

AB The invention provides a pharmaceutically elegant solid oral formulation of olanzapine and a process for making such formulation. The formulation comprises olanzapine as an active ingredient intimately mixed with a bulking agent, binder, disintegrant, and a lubricant; wherein such solid oral formulation is coated with a polymer selected from the group consisting of hydroxypropyl Me cellulose, sodium CM-cellulose, hydroxypropyl cellulose, polyvinylpyrrolidone, dimethylaminoethyl methacrylate-Me acrylate copolymer, Et acrylate-Me methacrylate copolymer, Me cellulose, and Et cellulose. A tablet contained olanzapine 1, lactose 67.43, hydroxypropyl cellulose 3.4, Crospovidone 4.25, microcryst. cellulose 8.5, Mg stearate 0.42, hydroxypropyl Me cellulose (as subcoating agent) 1.7, color mixture (as coating agent) 3.47 mg/tablet, Carnauba wax (as polishing agent) trace, and edible Blue ink (for imprinting) trace.

IT 132539-06-1P, Olanzapine
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oral olanzapine formulation)

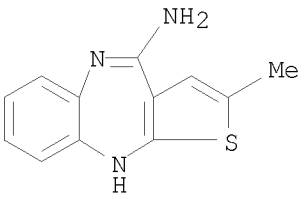
RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(oral olanzapine formulation)

RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



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OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

L31 ANSWER 61 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:656468 CAPLUS
DOCUMENT NUMBER: 125:301028
ORIGINAL REFERENCE NO.: 125:56347a,56350a
TITLE: Preparation of olanzapine solvates
INVENTOR(S): Bunnell, Charles Arthur; Hendriksen, Barry Arnold; Hotten, Terrence Michael; Larsen, Samuel Dean; Tupper, David Edward
PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Lilly Industries Ltd.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 733634	A1	19960925	EP 1996-301999	19960322
EP 733634	B1	20001122		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5631250	A	19970520	US 1995-410474	19950324
US 5703232	A	19971230	US 1996-586431	19960116
EG 24221	A	20081110	EG 1996-253	19960312
WO 9630374	A1	19961003	WO 1996-US3854	19960322
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9652578	A	19961016	AU 1996-52578	19960322
AU 9654279	A	19961016	AU 1996-54279	19960322
AU 706471	B2	19990617		
GB 2313835	A	19971210	GB 1997-19819	19960322
GB 2313835	B	19980916		
DE 19681286	T0	19980402	DE 1996-19681286	19960322
BR 9607790	A	19980707	BR 1996-7790	19960322
JP 11502535	T	19990302	JP 1996-529532	19960322
HU 9802824	A2	19990628	HU 1998-2824	19960322
HU 9802824	A3	20000128		
HU 224989	B1	20060529		
AT 9609021	A	20000115	AT 1996-9021	19960322
AT 406771	B	20000825		
IL 117613	A	20000716	IL 1996-117613	19960322
AT 197711	T	20001215	AT 1996-301999	19960322
ES 2151991	T3	20010116	ES 1996-301999	19960322
EE 3489	B1	20010815	EE 1997-232	19960322
PL 183723	B1	20020731	PL 1996-322501	19960322
CZ 292688	B6	20031112	CZ 1997-3000	19960322
RO 118872	B1	20031230	RO 1997-1761	19960322
SK 284143	B6	20041005	SK 1997-1218	19960322
IN 1996CA00516	A	20060707	IN 1996-CA516	19960322
SE 9703205	A	19970905	SE 1997-3205	19970905
FI 9703750	A	19970922	FI 1997-3750	19970922
NO 9704365	A	19970922	NO 1997-4365	19970922
NO 314663	B1	20030428		

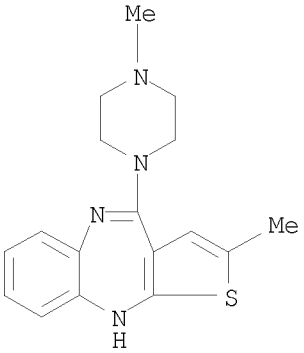
DK 9701089	A	19971112	DK 1997-1089		19970923
IN 1999CA00383	A	20050311	IN 1999-CA383		19990423
GR 3035355	T3	20010531	GR 2001-400180		20010202
PRIORITY APPLN. INFO.:			US 1995-409566	A	19950324
			US 1995-410474	A	19950324
			IN 1996-CA514	A3	19960322
			WO 1996-US3854	W	19960322
			WO 1996-US3917	W	19960322

AB The invention provides MeOH, EtOH, and PrOH solvates of olanzapine with improved properties characterized by x-ray spectra.

IT 132539-06-1P, Olanzapine
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of olanzapine solvates)

RN 132539-06-1 CAPLUS

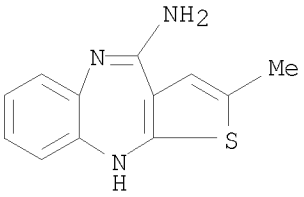
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of olanzapine solvates)

RN 138564-60-0 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (23 CITINGS)

L31 ANSWER 62 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:644040 CAPLUS
DOCUMENT NUMBER: 125:275918
ORIGINAL REFERENCE NO.: 125:51613a,51616a
TITLE: Preparation of crystalline olanzapine
INVENTOR(S): Bunnell, Charles Arthur; Hendriksen, Barry Arnold; Larsen, Samuel Dean
PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Lilly Industries Ltd.
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 733635	A1	19960925	EP 1996-302000	19960322
EP 733635	B1	20010816		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EG 23659	A	20070326	EG 1950-2	19960321
CA 2214005	A1	19961003	CA 1996-2214005	19960322
CA 2214005	C	20010703		
WO 9630375	A1	19961003	WO 1996-US3917	19960322
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9652578	A	19961016	AU 1996-52578	19960322
AU 9654279	A	19961016	AU 1996-54279	19960322
AU 706471	B2	19990617		
ZA 9602342	A	19970922	ZA 1996-2342	19960322
ZA 9602344	A	19970922	ZA 1996-2344	19960322
GB 2313835	A	19971210	GB 1997-19819	19960322
GB 2313835	B	19980916		
DE 19681286	T0	19980402	DE 1996-19681286	19960322
CN 1179160	A	19980415	CN 1996-192775	19960322
CN 1065536	C	20010509		
BR 9607790	A	19980707	BR 1996-7790	19960322
JP 11502535	T	19990302	JP 1996-529532	19960322
HU 9802824	A2	19990628	HU 1998-2824	19960322
HU 9802824	A3	20000128		
HU 224989	B1	20060529		
AT 9609021	A	20000115	AT 1996-9021	19960322
AT 406771	B	20000825		
AP 828	A	20000428	AP 1997-1065	19960322
W: KE, LS, MW, SD, SZ, UG				
CH 690579	A5	20001031	CH 1997-2245	19960322
EP 1095941	A1	20010502	EP 2000-203573	19960322
EP 1095941	B1	20031008		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
TW 442488	B	20010623	TW 1996-85103500	19960322
EE 3489	B1	20010815	EE 1997-232	19960322
IL 117610	A	20010826	IL 1996-117610	19960322

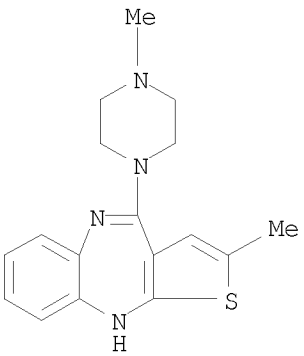
AT 204280	T	20010915	AT 1996-302000	19960322
ES 2159346	T3	20011001	ES 1996-302000	19960322
PL 183723	B1	20020731	PL 1996-322501	19960322
TW 513432	B	20021211	TW 1996-85103499	19960322
AT 251627	T	20031015	AT 2000-203573	19960322
CZ 292688	B6	20031112	CZ 1997-3000	19960322
RO 118872	B1	20031230	RO 1997-1761	19960322
ES 2208220	T3	20040616	ES 2000-203573	19960322
EP 1445259	A1	20040811	EP 2003-77455	19960322
EP 1445259	B1	20060628		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, AL				
SK 284143	B6	20041005	SK 1997-1218	19960322
IN 1996CA00514	A	20050304	IN 1996-CA514	19960322
AT 331719	T	20060715	AT 2003-77455	19960322
ES 2266719	T3	20070301	ES 2003-77455	19960322
SE 9703205	A	19970905	SE 1997-3205	19970905
LV 12018	B	19980920	LV 1997-163	19970908
LT 4349	B	19980525	LT 1997-148	19970916
FI 9703750	A	19970922	FI 1997-3750	19970922
NO 9704365	A	19970922	NO 1997-4365	19970922
NO 314663	B1	20030428		
DK 9701089	A	19971112	DK 1997-1089	19970923
HK 1013988	A1	20020705	HK 1998-115175	19981223
IN 1999CA00383	A	20050311	IN 1999-CA383	19990423
PRIORITY APPLN. INFO.:			US 1995-409566 A	19950324
			US 1995-410474 A	19950324
			EP 1996-302000 A3	19960322
			EP 2000-203573 A3	19960322
			IN 1996-CA514 A3	19960322
			WO 1996-US3854 W	19960322
			WO 1996-US3917 W	19960322

AB The invention provides a pharmaceutically elegant stable polymorph of olanzapine by precipitation from EtOAc.

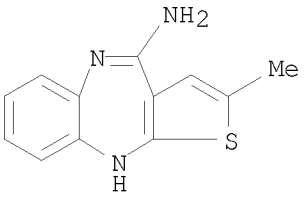
IT 132539-06-1P, Olanzapine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of crystalline olanzapine)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



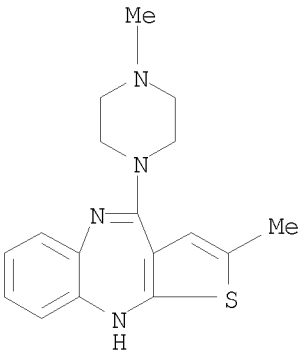
IT 138564-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of crystalline olanzapine)
RN 138564-60-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



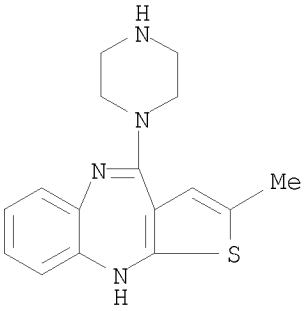
● HCl

OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)

L31 ANSWER 63 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:346664 CAPLUS
DOCUMENT NUMBER: 125:75193
ORIGINAL REFERENCE NO.: 125:14015a,14018a
TITLE: Analysis and pharmacokinetics of olanzapine (LY170053) and two metabolites in rat plasma using reversed-phase HPLC with electrochemical detection
AUTHOR(S): Chiu, Jenting Andre; Franklin, Ronald B.
CORPORATE SOURCE: Lilly Res. Labs., Eli Lilly Co., Indianapolis, IN, 46285, USA
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (1996), 14(5), 609-615
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A sensitive HPLC assay for measurement of the antipsychotic drug, olanzapine, in plasma has been developed. The assay has a limit of quantitation of 1 ng/mL in plasma and utilizes solid-phase extraction and electrochem. detection. The method provides a linear response for olanzapine over a concentration range of 1-100 ng/mL with coeffs. of determination greater than 0.9912. The inter-assay precision was 15.9% at the limit of detection and ranged from 7.33% to 8.45% over the range of 5-100 ng/mL. The intra-assay precision was in the range 0.97%-26.0%. The inter-assay accuracy ranged from 98.9 to 118% and the intra-assay accuracy ranged from 92.5% to 125% of the theor. value. In addition, the assay was extended to measure the plasma levels of two metabolites of olanzapine, namely the N-desmethyl- and the 2-hydroxymethyl analogs. The utility of the assay was demonstrated following the administration of a single oral dose of 14C-olanzapine to rats where, at several time-points after dosing, the plasma was assayed for total radioactivity, levels of olanzapine, and the two metabolites. Olanzapine and two of its metabolites accounted for less than 50% of the total plasma radiocarbon; olanzapine accounting for approx. 39% at the Cmax, N-desmethyl for 5% and 2-hydroxymethyl for 8% resp. The plasma elimination half-times for olanzapine and the two metabolites were approx. the same, ranging from 3.3 to 4.4 h.
IT 132539-06-1, Olanzapine 161696-76-0, LY 170055
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(anal. and pharmacokinetics of olanzapine (LY170053) and two metabolites in rat plasma using reversed-phase HPLC with electrochem. detection)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

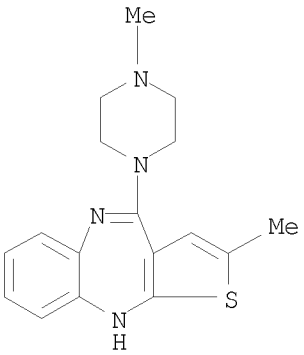


RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)

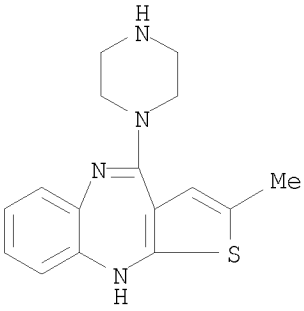


OS.CITING REF COUNT: 37 THERE ARE 37 CAPLUS RECORDS THAT CITE THIS RECORD (37 CITINGS)

L31 ANSWER 64 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:112754 CAPLUS
DOCUMENT NUMBER: 124:219304
ORIGINAL REFERENCE NO.: 124:40213a,40216a
TITLE: Identification of the human cytochromes P450 responsible for the in vitro formation of the major oxidative metabolites of the antipsychotic agent olanzapine
AUTHOR(S): Ring, Barbara J.; Catlow, John; Lindsay, Thomas J.; Gillespie, Todd; Roskos, Lorin K.; Cerimele, Benito J.; Swanson, Steven P.; Hamman, Mitchell A.; Wrighton, Steven A.
CORPORATE SOURCE: Lilly Research Laboratories, Lilly Corporate Center, Eli Lilly and Company, Indianapolis, IN, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1996), 276(2), 658-66
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The formation kinetics of 2-hydroxymethyl olanzapine (2-OH olanzapine), 4'-N-oxide olanzapine (N-O olanzapine) and 4'-N-desmethyl olanzapine (NdM olanzapine) were analyzed in vitro. Biphasic kinetics were observed for formation of 2-OH and NdM olanzapine. The high-affinity enzyme responsible for 2-OH olanzapine formation by two human liver samples exhibited an intrinsic clearance (CLint) of 0.2 μl/min/mg. NdM olanzapine formation by two human liver samples exhibited a CLint of 1.0 μl/min/mg for the high affinity enzyme. The formation of N-O olanzapine was linear up to 300 μM olanzapine, yielding a CLint of 0.32 to 1.70 μl/min/mg. The formation of 7-hydroxy olanzapine (7-OH olanzapine) exhibited an apparent Km of 24.2 μM. The rates of 2-OH olanzapine formation correlated with CYP2D6 levels and activity, and it was formed to the greatest extent by cDNA-expressed CYP2D6. N-O olanzapine formation correlated with human liver flavin-containing monooxygenase (FMO3) levels and activity. NdM olanzapine and 7-OH olanzapine formation correlated with CYP1A2 catalytic activities and they were formed to the greatest extent by expressed CYP1A2. These results suggest that CYP1A2 catalyzes NdM olanzapine and 7-OH olanzapine formation, CYP2D6 catalyzes 2-OH olanzapine formation and FMO3 catalyzes N-O olanzapine formation.
IT 132539-06-1, Olanzapine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(identification of the human cytochromes P 450 responsible for the in vitro formation of the major oxidative metabolites of the antipsychotic agent olanzapine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



IT 161696-76-0, LY 170055
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(identification of the human cytochromes P 450 responsible for the in vitro formation of the major oxidative metabolites of the antipsychotic agent olanzapine)
RN 161696-76-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 121 THERE ARE 121 CAPLUS RECORDS THAT CITE THIS RECORD (121 CITINGS)

L31 ANSWER 65 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1992:83703 CAPLUS
DOCUMENT NUMBER: 116:83703
ORIGINAL REFERENCE NO.: 116:14259a,14262a
TITLE: Preparation of 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno-[2,3-b][1,5]benzodiazepine
INVENTOR(S): Chakrabarti, Jiban Kumar; Hotten, Terrence Michael; Tupper, David Edward
PATENT ASSIGNEE(S): Lilly Industries Ltd., UK
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 454436	A1	19911030	EP 1991-303679	19910424
EP 454436	B1	19950913		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 9175186	A	19911107	AU 1991-75186	19910422
AU 643267	B2	19931111		
IL 97912	A	19951031	IL 1991-97912	19910422
IL 112575	A	19990817	IL 1991-112575	19910422
CA 2041113	A1	19911026	CA 1991-2041113	19910424
CA 2041113	C	19980714		
FI 9101986	A	19911026	FI 1991-1986	19910424
FI 101379	B1	19980615		
NO 9101624	A	19911028	NO 1991-1624	19910424
NO 178766	B	19960219		
NO 178766	C	19960529		
CN 1056693	A	19911204	CN 1991-103346	19910424
CN 1028429	C	19950517		
HU 60503	A2	19920928	HU 1991-1372	19910424
HU 212416	B	19960628		
ZA 9103085	A	19921230	ZA 1991-3085	19910424
JP 07089965	A	19950404	JP 1991-228215	19910424
JP 2527860	B2	19960828		
CZ 279937	B6	19950913	CZ 1991-1168	19910424
ES 2078440	T3	19951216	ES 1991-303679	19910424
SK 279196	B6	19980708	SK 1991-1168	19910424
KR 195566	B1	19990615	KR 1991-6544	19910424
RU 2043992	C1	19950920	RU 1992-5052762	19920925
LV 10262	B	19950420	LV 1993-517	19930608
FI 9701316	A	19970327	FI 1997-1316	19970327

PRIORITY APPLN. INFO.: GB 1990-9229 A 19900425
IL 1991-97912 A3 19910422
FI 1991-1986 A 19910424

OTHER SOURCE(S): MARPAT 116:83703

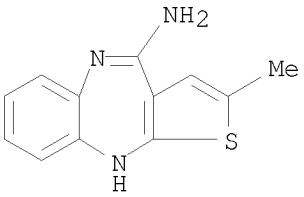
AB Title compound (I) useful for treatment of a disorder of the central nervous system (no data) was prepared 4-Amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine-HCl (preparation given) was refluxed in N-methylpiperazine, DMSO and MePh, under N atmospheric for 20 h to give I. Pharmaceutical formulations containing I are given.

IT 138564-60-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of nervous system agent)

RN 138564-60-0 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepin-4-amine, 2-methyl-, hydrochloride (1:1) (CA INDEX NAME)



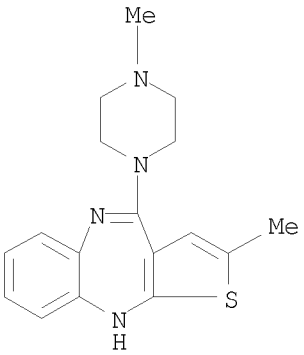
● HCl

IT 132539-06-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as nervous system agent)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 22 THERE ARE 22 CAPLUS RECORDS THAT CITE THIS RECORD (30 CITINGS)